Vol. 66, No. 10 Established 1884 October 1949

ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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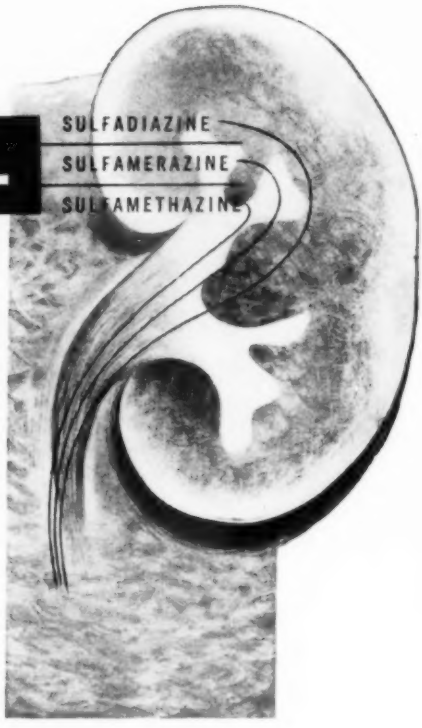

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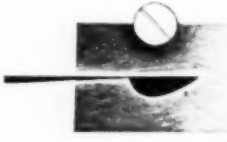

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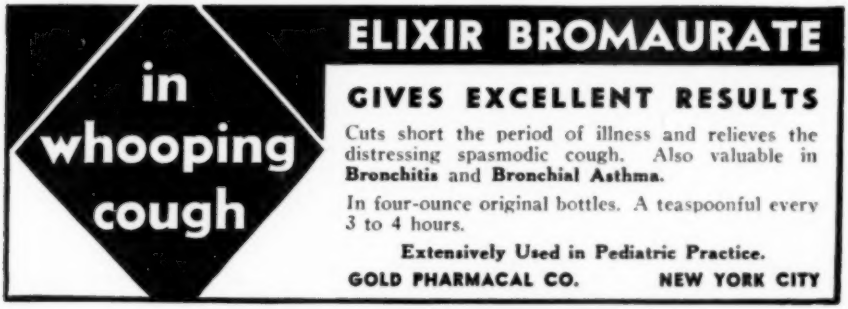
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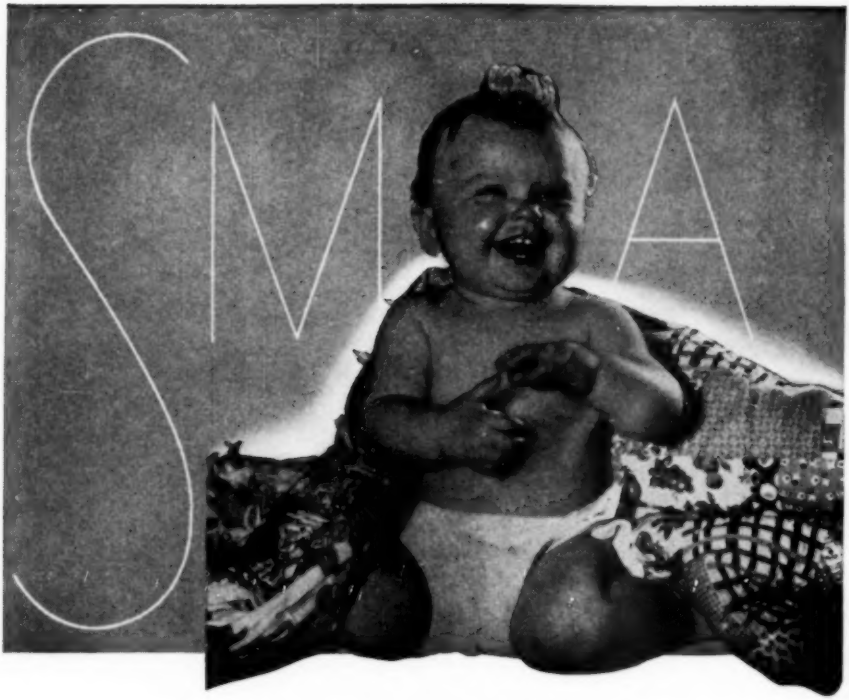

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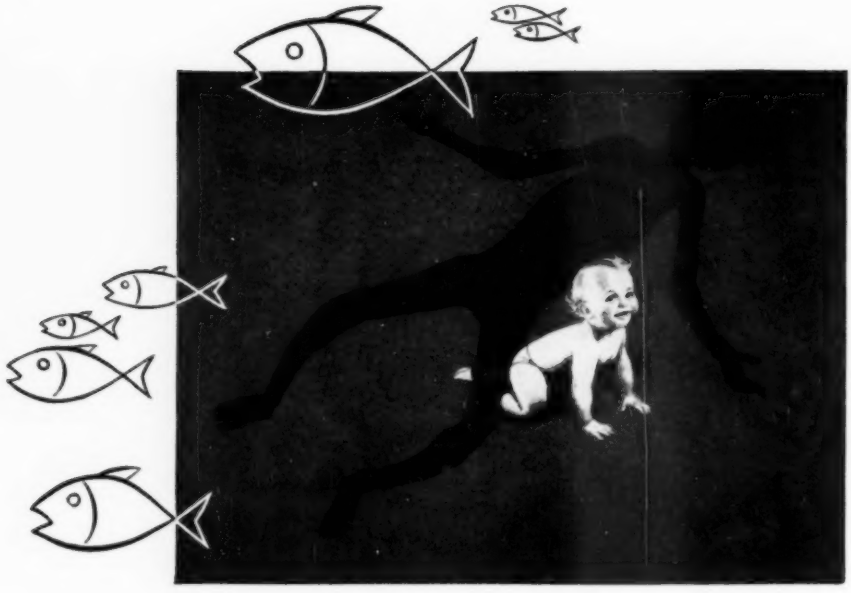

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RECURRENT PAROXYSMAL TACHYCARDIA IN INFANCY*

FREDERICK K. SARGENT, M.D.,

AND

JAMES B. GILLESPIE, M.D.

Urbana, Ill.

The difficulties in diagnosis and the danger of overlooking paroxysmal tachydardia in the young infant justify the report of a single case of this unusual entity. The reported case is of particular interest because of the rapid rate of the tachycardia, the associated anemia, and the inability to control the attacks with dosages of digitalis alone.

Taran and Jennings[1], in 1937, published one of the first comprehensive reviews of the literature in connection with their report of the syndrome in a seven-day-old infant. In a review of 52 cases, reported between 1892 and 1935, in patients four days to fifteen years of age, it was noted that males and females were equally affected; in the author's opinion, quinine was not effective and digitalis was the drug of choice though its use was fraught with danger because of possible ventricular fibrillation.

Hubbard[2], in 1941, presented the classical study of paroxysmal tachycardia in infancy. He reported 9 cases; the fact that 6 of these were seen in a one-year period indicates that the condition is not as rare as has been supposed. He reviewed 28 cases including his own and came to the conclusion that quinidine was

*From the Department of Pediatrics, Carle Memorial Hospital and Carle Hospital Clinic, Urbana, Illinois.

of no value in treatment of the condition but that digitalis in adequate dosage was of definite assistance in controlling the tachycardia. Acetyl-beta methylcholine bromide (mecholyl) was tried and caused circulatory failure in one patient. It was concluded that mecholyl should only be used when all other treatments fail. Six of the 28 cases recovered spontaneously, and 14 recovered after digitalis. The highest rate noted in this series was 305. The author pointed out that pneumonia and congenital idiopathic hypertrophy of the heart were among the common faulty diagnoses and that the condition, if allowed to persist, may well lead to congestive failure.

Hubbard and Starbuck[3] later reported a case in an infant two months of age whose cardiac rate reached 353. This patient was controlled with three one-half cat unit doses of digitalis and made a complete recovery.

There have been numerous subsequent reports concerning the good response with digitalis. Hobbs[4] reported the case of a two-month-old infant who was well controlled with digitalis. Howard[5] and Schieve[6] reported single cases which responded well to digitalis. Scott and Limper[7], in 1946, reported two cases, one of which recovered with digitalis while the other died after one attack had been stopped with quinidine.

CASE REPORT

S. T., a male infant, was born on August 14, 1947, at Carle Memorial Hospital. Birth weight was 3005 grams; both mother and baby were Rh negative. Jaundice was noted on the second day at which time the hemoglobin was 10.4 grams. He did well in the nursery and was discharged home on the sixth day with a weight of 3062 grams. Iron was prescribed at the time of dismissal from the hospital.

The infant was readmitted to the hospital at 11 days of age. He had been taking 45 cc. to 75 cc. of formula each four hours. On the morning of admission, he had awakened with rapid, grunting respirations, and irritability; all day he had refused feedings, and he vomited just once prior to admission.

On admission the rectal temperature was 39°, respirations were 60 per minute, and pulse was 200 per minute. The infant was pale, respirations were grunting, and the abdomen was distended.

Examination of the ears, nose and throat was noninforming; an area of decreased breath sounds over the right lower lung field was suspected. The initial working diagnosis was pneumonia or

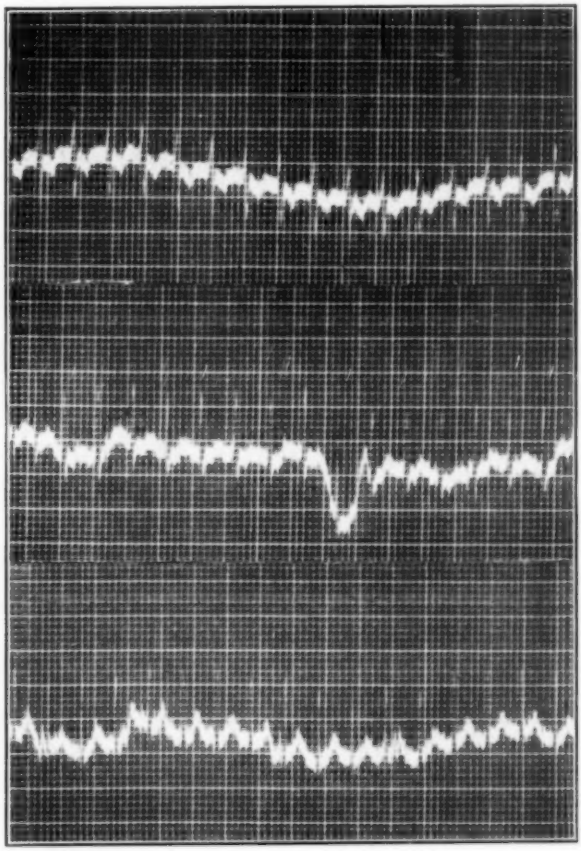

Fig. 1. Electrocardiogram of patient at six weeks of age showing paroxysmal auricular tachycardia with rate of 320 per minute.

anemia. The blood count revealed a hemoglobin of 6.95 grams, erythrocytes 2,210,000, leukocytes 11,390, with 70 polymorpho-

nuclear leukocytes, 27 lymphocytes, 1 eosinophil, 1 basophil and 1 nucleated red blood cell. A roentgenogram of the chest showed no significant pulmonary process. Parenteral penicillin (20,000 units) was started at three-hour intervals along with sodium sulfadiazine at 12-hour intervals; both were continued for three days. He received two blood transfusions during this period of hospitalization. Improvement occurred, and he became afebrile on the second day and remained so thereafter. The hospital course was marked by moderate edema of the hands, feet and face; the tachycardia noted on admission continued and was present at discharge on the fifth day. Hemoglobin increased to 12 grams after the transfusions.

The infant was seen at regular intervals after the above admission. He continued to do well except for being a poor feeder, never taking more than 75 cc. of formula and usually feeding at least an hour. At six weeks of age, his weight was 3.9 kg., and he had gained 255 grams in the previous two weeks.

On examination at six weeks of age, his color was slightly dusky with cyanosis upon crying; rapid respirations and tachycardia were present. Electrocardiogram revealed paroxysmal auricular tachycardia with a rate of 320 (Fig. 1.). He was readmitted to the hospital on September 24, 1947 for treatment of the tachycardia. The transverse diameter of the heart at this time was 4.5 cm. by roentgenogram. He was started on quinidine sulfate, .065 grams every hour for four doses. The tachycardia persisted after the quinidine with a rate of 240 on the second day. One cc. of digifoline (½ cat unit) was given without change in the rate; a second dose was administered in three hours without effect, and the third dose was given after another three-hour period. After the fourth dose of digifoline, or a total of 2 cat units of digitalis, the rate dropped to 108, and the infant appeared much improved. The next day the rate was 116, and, except for feeding poorly and some vomiting, he appeared to do well. Hemoglobin was 8 grams, and the infant was given 20 cc. of intramuscular blood. He continued to do well, except for the vomiting which improved with atropine and phenobarbital before feedings.

On the sixth day, the tachycardia recurred; at this time one dose of ½ cat unit of digitalis slowed the rate to 108. It was then decided to place the infant on a maintenance dose of digitalis in

an attempt to prevent recurrence of the tachycardia, and 5 drops of tincture of digitalis daily was started. Transverse diameter of the heart at this time was 6.5 cm. On the second day of maintenance dosages of digitalis, the infant required three one-half cat unit doses to break the recurring tachycardia. There was no recurrence of tachycardia for three days, at the end of which time maintenance dosage was increased to 5 drops two times daily. Tachycardia continued to recur frequently while the maintenance dosage was increased gradually to 8 drops of the tincture three times daily. On the twenty-third hospital day, quinidine, grains 2, three times daily was started, and the digitalis tincture was continued. After the start of the quinidine, there was no recurrence of the tachycardia; the infant gradually improved in ability to feed, and was discharged home on the thirty-sixth day with maintenance doses of both digitalis and quinidine. He received four blood transfusions, and the hemoglobin was 11.15 grams on dismissal.

There has been no recognized recurrence of the tachycardia in this patient; on December 2, 1947, roentgenograms of the chest showed the heart to be of normal size. He has continued to do well except for one febrile illness at the age of 3½ months, at which time all laboratory studies, including blood culture, blood urea, sedimentation rate, urinalysis, lumbar puncture and roentgenograms of the stomach and esophagus, were negative. At the age of 14½ months, both digitalis and quinidine were discontinued; the child weighed 9.9 kg., and he was developing normally. On May 9, 1949, when last observed at the age of 21 months, there had been no recurrence of the tachycardia, and he was in excellent health.

COMMENT

This patient presented a diagnostic problem because of the associated anemia. It may be pointed out that an electrocardiogram is almost essential for a diagnosis of this condition in early infancy.

Our experience with digitalis differed from that of most authors on this subject. It was effective in this patient in controlling the individual attacks but was ineffective in preventing recurrences when administered alone. It has been stated[8] that in all probability, if one "waits out" an attack, the attack will probably cease spontaneously. However, if an attack does not stop, congestive

failure may well follow; it seemed wise to prevent the tachycardia in this case. Several authors[9, 2] in discussing the use of mecholyl have suggested that this drug be used only if other recognized treatments fail. Mecholyl should be used with extreme caution; it may cause circulatory failure as it did in one of the cases reported by Hubbard[2]. Whenever used, atropine for control of circulatory failure should be readily available.

Little is known concerning the primary cause of the tachycardia in this syndrome. One case reported by Wegman and Egbert[10] was found at post-mortem to have a rhabdomyoma of the heart. An unusual case reported by Garvin and Kline[11] was recognized three months prior to birth at term. Another reported case by Kimball and Burch[12] was found to have two aberrant bundles of cardiac muscle tissue. It is difficult to determine whether or not the anemia was a factor in the great tendency to recurrence of tachycardia in our patient. It seemed obvious that quinidine was of definite value in preventing recurrences of the tachycardia in this patient.

SUMMARY

The literature of paroxysmal tachycardia in infancy has been briefly reviewed, and the case of an infant six weeks of age in whom recurrences were frequent has been presented. Digitalis was effective in controlling the individual attacks and together with quinidine was effective in preventing recurrences. The ease of overlooking this condition in young infants had been emphasized.

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TREATMENT OF ANTERIOR POLIOMYELITIS*

Report on Intraspinal Administration of Pyridoxine and Thiamine Hydrochloride and Artificial Fever Therapy

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All recently introduced methods of treatment in anterior poliomyelitis, including the Kenny treatment[1], neostigmine[2] and curare [3], have been aimed mainly at the peripheral manifestation of the disease. It was generally assumed that the pathological changes in the spinal cord were probably irreversible after the infection had set in, and that unless a specific agent was found effective in the preparalytic or early paralytic stages, no treatment would be of value as far as affecting the changes in the central nervous system. The protagonists of Sister Kenny[4] have tried to minimize the importance of cord damage in anterior poliomyelitis by placing special stress on "muscle spasm" as the most important factor in causation of pain in the acute stage and in the formation of deformities in later stages in cases not treated according to the Kenny method. However, later studies[5] have proven that the so-called "muscle spasm" is not really the most damaging symptom of the disease and that the pathology in the nervous system is directly responsible for the "muscle spasm" as well as the paralysis.

It has been previously suggested[6] that the changes in many of the cells in the spinal cord in the early stages of the disease were not anatomical but biochemical in nature. After invasion by the virus, the internal milieu of these nerve cells is disturbed, and the cell for a time is in a state of disrupted metabolism. These cells are not dead, but still unable to perform their function properly. The restoration of function in these cells as a result of improved metabolism would help explain the rapid recovery observed in some cases after what appeared, at the time of onset to be a moderately severe paralysis. It is probable that the affected cells require greater amounts of certain substances to enable them to metabolize at a more normal level of activity. These substances in our present state of knowledge include

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selected factors of the vitamin B complex[7], probably vitamin C[8], and the tocopherols[9]. Thiamine has been demonstrated by Peters[10], and Sherman and Elvehjem[11] to be of definite value in restoring brain tissue metabolism to normal in polyneuritic animals by improving oxygen uptake and aiding in removal of pyruvic and lactic acid substrates. Wintrobe[12] has demonstrated that pyridoxine is also an important factor in nerve tissue metabolism and that its absence from the diet will produce sensory neurone degeneration and paralysis in certain experimental animals. He has also suggested that it is the lack of several vitamin B factors rather than that of a single factor that is responsible for the nerve degeneration in cases of neuropathy which were in the past ascribed to thiamine deficiency alone.

I have previously described the results obtained from intraspinal administration of thiamine hydrochloride[13] and pyridoxine hydrochloride[14] when administered alone, or in combination with artificial fever, in cases of anterior poliomyelitis and other nervous system disorders. The pyridoxine and thiamine were administered for their nonspecific effect on nerve cell metabolism and not because a deficiency of these substances was suspected to be the cause of the disorder. The intraspinal method of administration was considered preferable in view of its previously demonstrated safety[15] and the advantages of placing these substances in greater concentration within the central nervous system. At first thiamine alone was used, but when it was found that pyridoxine was even more effective in relieving neuritic symptoms than thiamine, it was used instead and later combined with the former. Since 1944, thiamine and pyridoxine have been administered simultaneously intraspinally and their action appeared to be synergistic and more effective than if each were administered separately.

The artificial fever[16] was used for its nonspecific effect in relieving vascular spasm and muscle pain and for the increased oxygenation it produced in the central nervous system as a result of augumented blood flow and increased oxygen saturation of blood.

PATIENTS TREATED

Only patients with severe involvement of one or more extremities and those with pronounced muscle tenderness associated with

muscle weakness were selected for treatment. Several of the patients in this group have been treated elsewhere with hot fomentations for varying periods of time and were transferred for intraspinal and artificial fever therapy after the former treatments failed to relieve the pain and spasm or produce appreciable increase in muscle strength. Nonparalytic cases and cases with transient muscular weakness and discomfort on motion, which could be adequately controlled by analgesics, were not included in this group. The latter cases required no treatment other than bed rest, ample vitamin intake, and local infra-red or inductothermy heat applications during the acute phase.

A total of 38 patients have been treated either by intraspinal therapy alone or intraspinal therapy combined with artificial fever. Eighteen patients received intraspinal therapy alone and twenty patients received intraspinal therapy combined with artificial fever. Six patients in the latter group were treated in 1944, and 14 patients during the epidemic in 1946, when a total of 188 cases of poliomyelitis were reported in the state. Up to the present, 34 patients have received artificial fever therapy for anterior poliomyelitis.

The largest number of artificial fever treatments administered to a single patient was five. Several patients required only 2 treatments. The oldest patient was 36 years old, and the youngest patient 4 years. Three patients were in the respirator when removed for treatment, two with bulbospinal involvement, and one with severe intercostal and diaphragmatic paralysis and involvement of all extremities.

The age of the youngest patient to receive intraspinal therapy was 6 months. This patient had involvement of both lower and one upper extremity. The largest number of intraspinal treatments given to a single patient was seven. Three respirator cases received intraspinal therapy while in the respirator, and following each treatment the time these patients were able to remain out of the respirator was nearly doubled. One respirator case with involvement of all extremities was also pregnant. She received a total of 4 intraspinal treatments, three prior to delivery of a normal child, and one intraspinal and three artificial fever treatments after the delivery.

METHOD OF TREATMENT

The following method for intraspinal administration is being followed at the present time. A spinal puncture is carried out with patient usually lying on the more severely affected side. After the spinal fluid pressure is determined, 5-10 cc. of spinal fluid is removed, the amount withdrawn depending on the initial spinal fluid pressure, for cytological, total protein and sugar determinations. From sterile ampules, 15-25 mg. of pyridoxine (Hexa Betalin, Lilly) and 5-10 mg. of thiamine (Betaxin, Winthrop) in aqueous solution are aspirated in a 20 cc. sterile syringe and about 10 cc. of spinal fluid is gradually withdrawn into the syringe. Occasionally, due to blocking of the spinal needle opening by a nerve root, only 3-4 cc. of spinal fluid can be withdrawn at first. Turning the needle or slight change of patient's position will usually allow free withdrawal of additional fluid. The solution is slowly reinjected into the canal and gently barbotaged. There is no reaction to the intraspinal injection if at least 8-10 cc. of spinal fluid is used as a diluent. It was found, however, that when a lesser amount of spinal fluid is withdrawn, not infrequently a burning sensation over buttocks or in the extremity on which side patient was lying will be experienced by patient near the termination of the injection. This disappears, however, after the patient is changed to a prone position or turned to the opposite side and no ill effects have been observed following this reaction. The response to the treatment is frequently fairly rapid, so that within a few minutes after the injection is completed, some patients would comment that their extremities felt "ligther," "less heavy," "more natural," and that they could move them better. Objectively, resistance to straight leg raising is usually reduced after a treatment with some diminution of muscle pain and spasm, and range of voluntary movement is often noticeably increased in some of the less severely affected cases. The maximum improvement may not be reached, however, till several weeks have elapsed.

The artificial fever is administered by means of an inductotherm cabinet. The patient's temperature is gradually raised to 103°-104° F. and kept at this temperature for an hour or longer de-

pending on the patient's tolerance. During the induction period, the intermittent administration of oxygen was found to make the treatment less unpleasant and seemed to increase the patient's tolerance to the fever. Fruit juices, and water, to which salt had been added, is administered frequently in small amounts during the treatment. Each patient also receives 100-250 mg. ascorbic acid while in the cabinet, and also 10 grains of calcium lactate. The latter drug has been administered routinely after one patient developed mild hyperventilation tetany while in the fever cabinet which was rapidly relieved after the oral administration of the calcium lactate. There have been no unpleasant reactions from the artificial fever treatments, and several patients who received hot fomentation treatments previously have expressed preference for the former because of the shorter duration of the individual fever treatments, and the fewer treatments required to relieve the muscle tenderness and back rigidity. The youngest patient treated previously with artificial fever was 2½ years old and the youngest in the present group was 4 years old. Age, however, did not appear to be a contraindication to the treatment. In respirator patients the first treatment was usually of shorter duration, and if any signs of excessive fatigue appeared these patients were immediately removed from the fever cabinet and returned to the respirator.

All patients were also placed on oral mixed vitamins (ABCD) which included at least 150 mg. of ascorbic acid and 50-100 mg. of natural mixed tocopherols daily for adults, and wheat germ oil 1 cc. per 10 pounds of body weight in children[17]. In cases with bulbar involvement all medication and feeding were administered parenterally while acute bulbar symptoms persisted. None of the patients were immobilized during the acute stage, and pillow supports and splints were used whenever the orthopedic consultant felt it was indicated.

Physiotherapy, including passive movements, were begun as soon as the acute painful stage had subsided and pool treatment usually was started after the end of the quarantine period. Local gentle massage of extremities with wheat germ oil was found helpful in maintenance of normal skin texture.

RESULTS

The accurate evaluation of results from any form of treatment in a disease as varied in its manifestations as anterior poliomyelitis is rather difficult and unavoidably will be affected by the personal interests and subconscious bias of the attending physician. An attempt was made in this group to have each case evaluated by an orthopedic consultant shortly after the patient was admitted to the hospital, and to have him follow-up the patient in the hospital and also attend to patient's orthopedic needs following discharge. Muscle power evaluation by a competent physiotherapist were carried out following admission and at intervals during the patient's stay in the hospital. No harm was observed in any of the patients from such examinations if gently carried out, and it was very helpful in establishing an approximate extent of muscle involvement present even in the acute painful phase. I believe that such determinations more frequently applied would have eliminated many non-paralytic cases from having received unnecessary prolonged fomentation therapy, as the so-called "spasm" is, in most cases, a self-limited process and in the treated cases credit was thus given to the treatment method used rather than to the spontaneous termination of the painful stage. Usually such patients responded well to rest during quarantine period, oral vitamin therapy as described above and mild analgesics. None of the patients in the group were included in this study. No ill effects were observed following repeated spinal puncture, provided the fluid was removed slowly, and some relief of headache from this procedure alone was observed in cases where spinal fluid pressure was found to be increased on admission.

Of the 18 patients who received intraspinal therapy alone sixteen escaped without any residuals although all had moderately severe symptoms on admission. These included neck and back rigidity, muscular weakness in one or more extremities, and muscular tenderness. A number of patients in this group also displayed evidence of muscle "spasm," especially in their trapezii, hamstrings and quadriceps. None of them required any artificial fever therapy, and treatment consisted of intraspinal and oral vitamin therapy and physiotherapy. All patients in this group were given orthopedic clearance before discharge.

The patients in the combined artificial fever-intraspinal therapy group had severe involvement of two or more extremities, with five showing only zero to a trace of power in two or more extremities. Four of the patients required respirator care for varying periods of time. Twelve of these patients were placed under treatment while in the acute state and six did not receive treatment until several months after the initial infection had elapsed. It was found that the sooner after the onset of acute symptoms treatment was begun, the shorter the painful period and the greater the response to intraspinal therapy. Patients with no perceptible contractile muscle power several weeks after onset of acute symptoms showed the poorest response as far as return of muscle strength was concerned, while those patients with poor or fair power in affected muscles usually responded with gain of one or more points on the Lovett scale. All of the patients treated except one were ambulatory. This exception is a respirator case with complete quadriplegia and only perceptible movements in finger tips which was not referred for treatment until about four months had elapsed after the acute illness. He was able to remain out of the respirator about 15 minutes before the first intraspinal treatment. After each successive spinal treatment the time he was able to remain out was doubled, so that in the end he was able to remain 6-8 hours out of the respirator. Trace of movement in all extremities also became apparent after the intraspinal therapy. He was given only 2 fever treatments as he tolerated them rather poorly. However, in view of the extent of his paralysis and the minor gain in muscle power anticipated to result from additional fever treatments, it was not considered to be sufficiently worthwhile to warrant exposing patient to the strain.

Of three other patients who were nearly as severely affected as the above patient, who were placed under treatment within a few days after the onset of the illness, two are ambulatory, one with some residual involvement of both shoulder girdles and chest musculature, and one with involvement of both upper and one lower extremity. The third case with total quadriplegia after admission with only perceptible power in figures of one hand, has shown return of normal function in left upper extremity, fair function in left lower, a trace of power in right upper and a flail lower extremity. She is able to stand with aid, propel herself in

a wheel chair, has no muscle pain or rigidity and is still showing slow gain in muscle strength six months after the onset of the acute illness.

One of the respirator cases was in the fifth month of pregnancy, and required daily respirator care till after birth of a normal child. She had involvement of all extremities, early bulbar symptoms, and involvement of intercostal muscles. Intraspinal therapy was started while patient was in the respirator and she was able to remain out only about 30 minutes at the time of the first treatment. After each treatment the time she was able to remain out was doubled so that shortly before the time of the delivery she was able to remain 18 hours out of the respirator, although she required longer periods of respirator care for a few days before delivery. She was discharged from the hospital 8 months after admission, able to walk without aid and requiring no further respirator care, although still showing residual weakness of selected muscles of right upper and left lower extremities.

ILLUSTRATIVE CASE REPORTS

Case 1. C.P. This 23-year-old woman was transferred to the Elliot Hospital on February 16, 1944 for artificial fever and intraspinal therapy. She became ill in August 1943, with chills and elevation of temperature, and several days later developed speech difficulty, was unable to swallow solids, and regurgitated liquids through her nose. The following day paralysis of left upper extremity developed. The next day the right upper extremity became involved, and two days later, both lower extremities become paralyzed. She received some hot fomentation treatments and physiotherapy elsewhere with some improvement in condition of upper extremities, but with little change for the better in the lower. Her dysphagia had disappeared, and speech also improved, but the paralysis remained unchanged.

On admission she had pronounced rigidity of back and lower extremities. She was unable to sit up unsupported or turn over without assistance. She had poor to fair power in latissimus dorsi, good power in biceps, poor in triceps, fair power in supinators and fair to good power in small muscles of hands. Poor to fair power was present in gluteals, poor in hip flexors, fair in rotators, poor to fair in hip abductors and adductors, poor in quadriceps and hamstrings, poor to fair in gastrocnemii, poor in anterior tibials and other muscles of leg and foot. Both lower extremities were atrophied and passive movement was painful.

She was given 50 mg. pyridoxine and 20 mg. thiamine on Feb-

ruary 19, 1944, on February 28, 1944, and on March 3, 1944. She also received five artificial fever treatments, on February 24, 1944, March 3, 1944, March 10, 1944, and April 3, 1944. Mixed vitamins were administered orally, including 100 mg. of mixed tocopherols daily. Physiotherapy was administered by same physiotherapist who cared for her at the other hospital. After the second fever treatment she was able to turn over without assistance, and after the third treatment she was able to walk with the aid of a cane. After the fifth treatment she was able to walk short distances without a cane.

At the time of her discharge all her movements were free and there was no residual tightness or back rigidity. All muscles have gained one or more points on the Lovett scale, so those which were poor became fair to good, and those that were fair became good to normal. Six months after her discharge she was found to have continued to gain, was able to do all her housework, walk in public without aid of cane or braces.

A year later she was gainfully employed as a waitress. Strength in lower extremities was good to normal, but she still has residual weakness of abductors of shoulders and some atrophy of shoulder girdle muscles.

In view of the extensive paralysis and bedridden state on admission after seven months of hot fomentation treatments and physiotherapy, her progress appeared very satisfactory after four weeks of intraspinal and artificial fever therapy. Increase in range of movements and improvement in muscle strength was noticeable after each treatment, and it appeared that while the artificial fever treatments were more instrumental in producing relief from rigidity and pain, the intraspinal therapy was more effective in producing the gain in muscle power.

Case 2. E. L. This 13-year-old boy was admitted to the Elliot Hospital on September 7, 1946 after three days of illness at home. On admission he had pronounced rigidity of neck, back and extremities, and he held himself in a position of opisthotonus. There was a bilateral Kernig. Both lower extremities were affected. The only movement present in right lower extremity was that of dorsiflexion of toes. He was able to flex left thigh and extend left leg with assistance. Deep reflexes were absent. All movements, however, were extremely painful and patient would scream when approached to be turned or bed clothes changed. He received hot fomentation treatments from the day of admission to September 14, 1946. On that day, because of his failure to receive appreciable relief from the hot fomentations, he was given 30 mg. of pyridoxine and 20 mg. thiamine intraspinally. He remained

in a position of opisthotonus during puncture with legs nearly extended because of rigidity of back muscles. Within a few minutes following the intraspinal injection, he was able to move his left lower extremity without discomfort, and without assistance. He also moved his right foot and toes voluntarily which he was unable to do before the medication was administered. The next day the pain was much less severe, and he moved left lower extremity without discomfort and he was able to flex his right thigh and leg. Neck rigidity was also less noticeable, although back still was held rigid. Skin also appeared dry and showed erection of papillae. Muscles were still tender to pressure. On September 17 he was given an artificial fever treatment with a total of three hours of temperature over 101° F. and a maximum temperature of 104° F. Following the treatment, range of movements of extremities was increased, his muscles showed better tone, and all movements could be carried out without causing pain. The skin texture also appeared normal. Intraspinal therapy was repeated on October 10, and again on October 23, 1946. He also received a second artificial fever treatment on October 23. He was discharged from the hospital on October 26, 1946, after seven weeks hospitalization. At the time of his discharge he had no rigidity, all muscles were rated as normal except for the iliopsoas on right which was good to normal. All deep reflexes were present, but sluggish. There was no restriction of joint action, and according to the orthopedic consultant, he showed no residuals at time of his discharge. When rechecked six months later, he showed normal range of movements, and no evidence of any residual changes.

This case is of interest because of apparent severe involvement of both lower extremities and intense pain which persisted for a week following admission in spite of hot fomentation applications. Increase in range of muscle movement and muscle strength and some relief of pain and rigidity followed the first intraspinal treatment. The artificial fever treatments, however, were more effective in relieving the back rigidity and pain and also produced improvement in peripheral circulation and concomitant skin changes.

Case 3. A.N. This 24-year-old woman was admitted to the Elliot Hospital on December 29, 1943, after she developed an attack of anterior poliomyelitis seven weeks earlier. This was manifested in difficulty in swallowing, impairment of speech and muscular weakness. At the end of 10 days she had no appreciable muscle power in any of her extremities, had severe muscle pain and was unable to feed herself. In view of her failure to improve at home with hot fomentation treatments, she was transferred to the Elliot Hospital for intraspinal and artificial fever therapy.

On admission she spoke in a whisper. She was unable to turn over or feed herself. She showed marked rigidity of back, was unable to sit up, and legs could only be raised to about 45° from a resting position. There was a questionable hypesthesia to pin prick over outer and anterior aspects of both arms and forearms. Vibration and position sense were normal. Muscle examination: Power was poor in anterior neck muscles, poor in deltoids, normal to good in trapezii, poor in pectorals, poor in biceps, triceps and pronators; poor to fair power in flexors and extensors of wrists, good power in finger flexors, poor to fair power in muscles of hands, with symptoms more marked on right. Chest expansion was shallow and there was poor power in abdominal muscles. There was poor to fair power in hip abductors, adductors, quadriceps, gastrocnemii, posterior tibials and extensors and flexors of toes. All deep reflexes were absent, except for knee jerks on left. Abdominal reflexes were not elicited. All muscles were tender on pressure. She was unable to bring her hand to her mouth and had to be fed on admission.

She was given intraspinally 50 mg. of pyridoxine and 20 mg. of thiamine on December 30, 1943 and mixed vitamins orally including 100 mg. of mixed tocopherols daily. The next day the hypesthesia of forearms had disappeared and it was less noticeable over arms. Range of movement of lower extremities increased, and she was able to bring her hand to her mouth. Also muscular tenderness had nearly disappeared. She was given a second intraspinal treatment on January 5, 1944, and an artificial fever treatment on January 6, 1944. On January 10, 1944, she was able to feed herself, and was able to turn over voluntarily in bed with ease which she could not do formerly. After the second artificial fever treatment, she was able to sit up in bed without support, stand with some assistance, and feed herself. Back rigidity was less pronounced. After the third artificial fever treatment on January 19, 1944, she was able to get in and out of chair with assistance and also was able to take a few steps. On February 4, 1944, she was able to walk about 10 yards without aid.

On February 11, 1944, she was again given 50 mg. of pyridoxine and 10 mg. of thiamine intranspinally. She continued to gain after this treatment and was discharged on February 15, 1944, much improved. At the time of her discharge, all muscles had gained one or more points since admission. She had no back rigidity. Leg extension was near normal. She was able to feed herself, comb her hair, walk without assistance, and get in and out of a chair unaided. When rechecked six months later she had no residual paralysis, and was planning to return to her job as a hairdresser. A year later she reported by mail from Florida about her employment there as a hairdresser and of carrying on with her job in a normal fashion.

While the diagnosis of poliomyelitis made by the family physician was questioned at first in view of nearly symmetrical involvement of all muscles of body, the normal protein of 35 mg. on admission to the hospital, the failure to show any appreciable improvement after several months of treatment again did not exactly fit in with a Guillain-Barré syndrome. The fact that she was helpless on admission and responded rather rapidly to combined intraspinal and artificial fever therapy has been of interest in this case, and improvement was noted immediately after the first intraspinal treatments. The disappearance of rigidity became more evident, however, after the administration of artificial fever. This case probably belongs in the "neuritic" group of poliomyelitis with the symptoms closely resembling the Guillain-Barré syndrome except for the absence of increased spinal fluid protein, persistent rigidity of back and extremities, and failure to show more rapid improvement as usually associated with cases of infectious polyneuritis.

Case 4. J. H. This 10-year-old boy was transferred to the Elliot Hospital on September 4, 1946, twenty-four hours after the onset of paralysis of lower extremities. He had a "cold" two weeks earlier from which he apparently recovered. Two days before admission, he complained of sharp pains in left knee, and he had a temperature of 100° F. Next day he complained of transitory pains in his abdomen and both knees and also in wrists. Later in the day he developed rigidity of his neck, complained of severe headache and pains in all extremities, and was unable to move his legs or void. A spinal puncture carried out elsewhere showed the presence of 17 leukocytes.

On admission he appeared severely ill with dry, hot skin and sordes around mouth. His neck was very rigid. Palate appeared higher on right side and uvula was pulled over to right. Right nasolabial fold appeared flattened out. He had a flaccid paraplegia with only to-and-fro movements of toes remaining. He was hyperestetic to pin prick and brush. All deep reflexes were absent. Muscles were tender to touch, and patient had to be handled very gently because of severe pain brought on by motion. He also appeared very irritable, cried very easily and presented a difficult nursing problem. He had to be catheterized on admission. He was placed on parenteral fluids because of early bulbar changes and difficulty in swallowing, intravenous vitamins B and C, and 200 mg. of mixed tocopherols intramuscularly daily. On September 7, the hyperesthesia in lower extremities had nearly disappeared and muscle tenderness was less pronounced. He con-

tinued, however, to complain of backache and the only perceptible movements were in the toes of left foot. He was given 50 mg. pyridoxine and 20 mg. thiamine intraspinally September 7, 1948. There was no unpleasant reaction to the injection, except for a slight burning sensation in left thigh which disappeared on change of position. Ten minutes after the injection was completed he remarked that the back pains had disappeared and it was also observed that some motion reappeared in left gastrocnemius and left tibialis anterior muscles.

He was given an artificial fever treatment on September 18, which he tolerated well. On September 19, he was completely free from pain, irritability and emotional instability which made him a nursing problem disappeared, and the range of movements increased in left foot. Passive movements were started in lower extremities. He received another intraspinal injection consisting of 40 mg. pyridoxine and 20 mg. of thiamine on October 2, 1946, and a third injection on October 23, 1946. He also received a second artificial fever treatment on September 23. He had no bladder symptoms following first intraspinal treatment. On September 30, he began pool treatments and was up and around in a wheel chair on October 10, 1946. He appeared very limber, there were no contractures, and he had fair power in left lower extremity while the right was flail. He remained in the hospital until November 16, 1946, mainly to receive additional pool treatments and await the fitting of braces. When rechecked six months later there was a trace of power in muscles of right lower extremity while all the muscles rated good in left lower. He was wearing a brace on one leg and was getting around with ease. One year later muscle power was good to normal in left lower extremity and there was a trace to poor power in right.

Case 5. G. M. This 31-year-old mother of four children was admitted to the hospital on August 24, 1946, after several days of illness at home. On admission, she had severe neck rigidity, and complained of headache and backache. She was unable to take any fluids by mouth because of sensation of drowning. Fundal vessels appeared congested, and there was an increase in light reflex. Nystagmoid movements were present in both eyes. Soft palate appeared higher on left. Tongue was coated, tremulous. There was pronounced weakness of muscles of all extremities although accurate examination could not be carried out because of severe discomfort on motion. Deep reflexes were increased, but there were no abnormal reflexes. She was unable to sit up and had much tenderness along spine. Patient was also five months pregnant at this time.

Spinal fluid studies on admission showed 523 polymorphonuclear leukocytes and 94 lymphocytes, a total protein of 83.3 mg. and sugar 94 mg.

On August 26, she showed definite respiratory embarrassment with great impairment of excursion of chest and her breathing was shallow, rapid and abdominal in character. She showed increased difficulty in swallowing, and gradually became more cyanotic. After she was placed in respirator and adjusted herself, the cyanosis disappeared. On August 26, 1946 an orthopedic examination could not be carried out satisfactorily because of patient's poor physical condition, but the consultant felt that no orthopedic treatment was indicated at this time and the prognosis in general was very poor.

Orthopedic recheck on September 14, 1946 showed that all muscles of respiration were paralyzed except for accessory neck muscles. Diaphragmatic action was not detected. Right upper extremity: Shoulder girdle muscle power poor to absent. Biceps fair, triceps absent. Flexors and extensors of wrists fair. Flexors and extensors of fingers poor to absent. Left upper extremity: Good except for poor deltoid and weakened shoulder girdle muscles. Abdominals absent. Right lower extremity: Good to normal. Left lower extremity: Foot good; knee extension poor; knee flexion good; muscle action on hip, poor to fair.

She was given 40 mg. of pyridoxine and 20 mg. of thiamine on October 2, 1946. Whereas previously she was able to remain out of the respirator only about 30 minutes, after the intraspinal medication she was able to remain out an hour and 35 minutes. The spinal fluid at this time showed 5 lymphocytes, a total protain of 31.2 mg. and 75 mg. spinal fluid sugar. She was given 25 mg. of pyridoxine and 25 mg. of thiamine again on October 22, 1946, and on November 14, 1946. She continued to show gradual gain and, following the last injection, was enabled to remain out of the respirator about 18 hours daily. She was able to feed herself, sit in a wheel chair and move head in all directions.

She was delivered of a normal child on January 14, 1947 by Dr. Benjamin P. Burpee, under light cyclopropane anaesthesia and control forceps after normal labor. She required brief respirator care before and after delivery. Her color remained good, however, and she was able to remain out of the respirator for 8 hours daily shortly before delivery and 12 hours after delivery.

Orthopedic recheck on February 1, 1947: Left upper extremity: All muscles were good except for poor apposition of thumb. Right upper extremity: Poor trapezius, deltoids and pectorals. Good latissimus dorsi. Poor triceps. Good extensors of digits and wrists. Fair finger flexors. All other flexor muscles of wrist and fingers poor to absent. There is slight contraction of both shoulders on abduction. Abdominals absent to poor. Left lower extremity: Hip flexors and knee extensors poor to fair. All other hip and knee muscles fair to good. Muscle action on

foot good. Equinus deformity of 100°. Right lower extremity: Muscles good to normal. Slight equinus deformity.

She received three artificial fever treatments on March 20, 1947, April 2, 1947 and on April 10, 1947, and also a subarachnoid injection of 25 mg. of pyridoxine and 10 mg. of thiamine on April 8, 1947, thirty-six hours before her last fever treatment. She was ambulatory then, required no respirator care and had been able to walk without aid.

She continued to gain and was discharged from the hospital ambulatory on May 3, 1947, after a hospitalization period of 8 months and 10 days.

COMMENT

Treatment in anterior poliomyelities still remains in a state of flux and depends in most instances on the personal preferences of the attending physician. However, since the introduction of the Kenny treatment, the total immobilization method of treatment, in vogue since 1916, has been replaced in most clinics by hot fomentations, alone or in combination with neostigmine therapy. The favorable reports on the use of curare by Ransohoff[18] has not been substantiated by Fox[19] and Richards, Elkin and Corbin[20] in a larger group of cases. Fox has also cautioned against the use of the drug as it may have deleterious effects, especially in bulbar cases. The favorable effect of neosigmine on the internuncial pool as reported by Kabat and Knapp[3] with the resultant relief of muscle spasm has been of interest academically, but the clinical results according to Spankus and Fox[21] have not been lasting or impressive. So far, however, most methods of treatment have been aimed at the peripheral manifestations of the disease, especially at the relief of the so-called "muscle spasm" which has been uncritically accepted by many following the introduction of the Kenny method as the most important cause of muscle weakness and deformities. The advantages of combined artificial fever-intraspinal vitamin therapy is that the effects are not limited to the relief of muscle spasm and pain, but that it also probably favorably influences the pathological changes in the spinal cord. Odom and McEachern[22] have found that thiamine deficiency in experimental animals will frequently unmask quiescent brain lesions and that the subarachnoid administration of thiamine will cause regression of these signs. It is also of interest that a defective breakdown of pyruvic acid in carbohydrate metabolism similar to that seen in animals deprived of thiamine was found by Meiklejohn, Passmore

and Peters[23] in cases of chloroform poisoning, partial asphyxia and insulin overdosage. This similarity of biochemical inadequacy in nerve cells brought on by noci of divergent origin brings up the possibility that similar biochemical impairment in cell metabolism may also exist in many nerve cells in the early stages of anterior poliomyelitis[24] and other neurotropic virus infections. The process is probably reversible in the early stages of the disease and if any therapy is going to be successful it will have to be aimed at improving the intracellular metabolism. The results from my own personal experience in treatment of cases with predominantly neuritic manifestations has proven intraspinal pyridoxine to be superior to thiamine in bringing on more rapid restoration of function. The beneficial effects were found not limited to anterior poliomyelitis, but were also observed in treatment of resistant cases of sciatic neuritis, cases of Guillain-Barré syndrome, alcoholic and other neuritides, and selected cases of multiple sclerosis. The results were even better when the pyridoxine and thiamine were administered simultaneously.

The action of the artificial fever is peripheral and central. In contrast to the hot fomentation, the inductothermy heat is deeper penetrating, and thus is more effective in relieving vasospasm and muscle tenderness, and in hastening absorption of intracellular and extracellular edema. Muscle tenderness was usually greatly relieved or completely disappeared after the second or third artificial fever treatment. It also increases the rate of blood flow and thus improved oxygenation is achieved in the brain and spinal cord, and also augumentation of removal of catabolic products. It is a safe procedure when properly supervised and none of the patients treated have shown any ill effects from its administration. The addition of vitamin C and sodium chloride during the treatment and intermittent oxygen inhalation has made it a safe procedure even in respirator cases.

It is of interest that in none of the patients treated was observed the residual vasomotor disturbances, contractures, or fibrotic changes so frequently seen in the past in extremities severely affected by poliomyelitis. Even in the most atrophic extremity the skin appeared warm and of normal texture. The absence of definite sensory changes, the lowered skin temperature of affected extremities, the dry skin, the muscle spasm and pain and

the disturbance of sweating mechanisms so often observed in cases of anterior poliomyelitis, would suggest a sympathetic origin for these symptoms. This most likely is a result of invasion by the virus of some of the sympathetic cells in the anterolateral horns of the cord in conjunction with other parts of the nervous system. The relief of such symptoms by sympathectomy[25] or paravertebral block[26] would also favor such an etiology.

The most pronounced improvement with intraspinal therapy alone was seen in the neuritic group of cases resembling a Guillain-Barré syndrome. Two or more intraspinal injections were sufficient to restore function rapidly in several such cases. The recovery in this group was undoubtedly due to the placement of the pyridoxine in direct contact with the affected nerve roots.

Relief of symptoms following intraspinal therapy was also observed in cases without definite paralysis, but with subjective complaints of weakness and exhaustion on moderate effort, and cramps of extremities after standing or walking short distances after these patients returned to their former activities. In chronic cases, with complete flaccid paralysis and flail extremities, the improvement was found to be minimal, although in several cases a trace of muscle power became apparent where previous no perceptible contractions were observed. The change in these cases was not sufficiently pronounced, however, to be considered significant.

Although several reports[27] have recently appeared dealing with increased susceptibility of certain experimental animals to poliomyelitis virus when placed on a thiamine enriched diet and prevention of paralysis by several dietary deficiencies, no exacerbation of symptoms were observed in any of the cases treated following pyridoxine-thiamine therapy even when used within a few days after the onset of the infection.

It is probable, even if one does accept the assumption that the above studies can be applied to humans, that the benefit derived by the affected nerve cells from the additional vitamins when supplied intrathecally and orally is sufficient to offset the damage supposedly produced as a result of increased susceptibility to virus spread produced by the thiamine.

SUMMARY AND CONCLUSIONS

Pyridoxine and thiamine hydrochloride were administered in-

traspinally to 38 patients with moderate to advanced muscle paralysis in the acute and subacute stages of anterior poliomyelitis. Twenty of the more severely affected patients also received two or more artificial fever treatments in combination with the subarachnoid vitamin therapy. All patients also received oral mixed vitamins, including 50-100 mg. of mixed tocopherols daily in adults and wheat germ oil, 1-4 cc, daily, in children.

Pyridoxine in doses of 20-35 mg. in adults and 5-10 mg. in children together with 5-10 mg. of thiamine for adults and 2-5 mg. in children, when diluted with spinal fluid, can be injected with safety into the spinal canal without producing any untoward reactions. Its administration resulted in appreciable gain in muscle power in nearly all cases, but was most effective in cases with predominantly neuritic symptoms, and cases with pronounced subjective weakness and residual fair to good muscle strength. In the less severely involved cases intraspinal therapy alone was sufficient to bring return of normal function in 16 of the 18 cases treated.

Artificial fever treatment with a temperature range of 103°-105° F. for one to three hours was well tolerated by all patients to whom it was administered except one respirator case who was given only two treatments because of poor tolerance. Its administration brought forth more rapid relief from muscle pain and reflex rigidity, produced improvement in general circulation and skin texture, and also aided in prevention of contractors and deformities.

The combined intraspinal vitamin therapy and artificial fever appeared to shorten appreciably the painful phase of the disease in the more severely paralyzed cases, hastened restoration of normal strength in weakened muscles, and thus effected reduction of hospitalization time and treatment costs. Intraspinal therapy alone, however, could be used effectively with other forms of treatment, such as hot fomentations, inductothermy heat, or immersion in a warm pool in cases with severe muscle spasm and pain, if facilities for fever therapy are unavailable. The results so far would indicate that it is the most promising method of treatment in poliomyelitis after paralysis had set in.

NOTE: The orthopedic care of these patients was under the supervision of Drs. Ezra A. Jones, Carl R. Friborg and Robert R. Rix of the orthopedic staff of the Elliot Hospital, Manchester, New Hampshire.

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FUNCTIONAL HYPOGLYCEMIA IN CHILDREN*

Report of Two Cases

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Hypoglycemic attacks in children are unusual, and reports in the pediatric literature are relatively few in number. Harris[1], in 1924, was one of the first authors to describe this syndrome, and Josephs[2], in 1926, was apparently the first author to report cases occurring in children. Rector and Jennings[3] presented eleven patients seen from 1930-34, and at that time they noted there were 35 reported cases of hypoglycemic convulsions in children. It apparently was spontaneous in 32 of them, while in two there were pancreatic adenomas and in one, hepatic insufficiency. Other authors have reported a small series of patients or single cases with hypoglycemic symptoms, but the literature has been confused by the lack of a standard definition, the complexity of the subject and the difficulty in determining the etiology of spontaneous hypoglycemia.

The purpose of this paper is to present two cases of functional hypoglycemia, and to compare them with a few of the previously reported cases, in an attempt to systematize the diagnosis and offer suggestions as to treatment.

CASE REPORTS

Case 1. B. P. was first seen at the Milwaukee Children's Hospital in September 1947 when he was about two years of age, with the complaint that he held objects close to his eyes in order to see.

The child was born after 8 months gestation and weighed 3½ pounds. After leaving the hospital, however, he seemed to develop normally. He had had a convulsion and a period of somnolence one year before the present admission, but had recovered spontaneously within 24 hours, and had had no recurrences. Parental histories were negative for syphilis, diabetes, tuberculosis and convulsions.

On admission examination, at this time, he had a slight

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asymmetry of the head. There were no external ocular muscle changes, but he had a bilateral zonular type of lens opacity, probably congenital in type. The remainder of the examination was normal, and he was sent home to be given an appointment for surgery.

He was next seen in August 1948 at three years of age, when, on the morning of admission, before eating breakfast, he had suddenly become drowsy, fallen asleep, and had remained so for one hour prior to admission. While being transferred to the hospital he had shaking movements of his arms and legs.

On examination he was comatose and could not be aroused even on stimulation. His temperature was 98° F., rectally. His pupils reacted sluggishly to light, and there were nystagmoid eye movements. The reflexes were absent and the Babinski test was positive on the left.

A spinal tap, done immediately, showed no pressure rise, 1 cell, 10 mgm.% protein and 29 mgm.% sugar. The blood sugar was 41 mgm.%, and the urine showed acetone and diacetic acid, but no sugar. The blood count was normal.

The child was given intravenous glucose, and he responded promptly. The following day the blood sugar was 67 mgm.%. X-ray examination of his wrists showed a normal bone age, and roentgenograms of the abdomen and skull were normal. The Mantoux test 1:10,000 was negative. A glucose tolerance test (capillary blood), after three days on a regular hospital diet, showed a fasting blood sugar of 97 mgm.%. 23.1 grams of glucose was then given by mouth and the following curve was obtained: ½ hour, 135 mgm.%; 1 hour, 118 mgm.%; 2 hours, 150 mgm.%; 3 hours, 112 mgm.%; 4 hours, 100 mgm.% He was discharged six days later on frequent feedings of a high carbohydrate diet.

He then remained well until November 10, 1948, when he suddenly became comatose. He had had regular meals the day before, but had eaten his supper at about three in the afternoon. At 6 P. M. he was drowsy and had slept until 9, and then he had become hyperactive. Four hours following this he once again became sleepy, and could not be aroused. He vomited several times but had no convulsions.

On examination, he was comatose with moderate neck rigidity and a temperature of 96.8° F. The remainder of the examination

was normal except for hyperactive reflexes and positive Kernig and Babinski tests.

A spinal tap revealed normal dynamics, one cell, 10 mgm.% protein, and 25 mgm.% sugar. The blood sugar was 34 mgm.%. 50 per cent glucose was given intravenously, and adrenalin subcutaneously. Within a matter of minutes he again was conscious. He was then placed on a standard hospital diet (140 grams of carbohydrate, 50 grams of protein and 70 grams of fat) for three days, and the glucose tolerance test was repeated. The fasting blood sugar was 104 mgm.% (capillary blood). 24.1 grams of glucose were then given by mouth and the following curve was obtained: ½ hour, 160 mgm.%; 1 hour, 145 mgm.%; 2 hours, 130 mgm.%; 3 hours, 87 mgm.%. Other blood chemistry revealed an NPN of 29.8 mgm.%, a total protein of 7.0 grams per 100 cc., blood cholestrol of 292 mgm.%, a prothrombin level 70 per cent of normal, and a normal Hanger liver function test. The urine was negative for urobilin.

The child was placed on a low carbohydrate diet for three days (50 grams of carbohydrate, 60 grams of protein and 110 grams of fat) and the glucose tolerance test was then repeated. The fasting blood sugar was 100 mgm.%. After 24.1 grams of glucose were given by mouth the following curve was obtained: ½ hour, 165 mgm.%; 1 hour, 155 mgm.%; 2 hours, 165 mgm.%; 3 hours, 63 mgm.%. At this time he became irritable, cried and was mentally confused. He was therefore fed, and his behavior promptly became normal.

He was diagnosed as a functional hyperinsulinism and was placed on a diet consisting of 70 grams of protein, 80 grams of fat and 75 grams of carbohydrate, and sent home. During the past six months on this diet he has had no further signs or symptoms of hypoglycemia.

Case 2. H. S. was first seen at the Milwaukee Children's Hospital when 20 months of age. The family history was unknown, as the child was a premature infant and had been adopted when he weighed two pounds. He was dusky following delivery and had a series of convulsions on the third day of life. He became cyanotic when taken out of oxygen, and physical examination suggested an atelectatic pneumonia. However, the chest x-ray appeared normal. The skull x-ray was not unusual, and the spinal fluid and blood count during the third month of life were normal.

The child appeared to be spastic at the time of hospital discharge, but during the intervening months he seemed to develop normally, and when seen at this hospital nothing unusual was noted on the physical examination, except tonsillitis and cervical adenitis. Treatment was symptomatic and improvement was rapid, and he was discharged after ten days' hospitalization.

Second hospital admission: He was well for the next three months until he had a sudden early morning generalized afebrile convulsion. Admission physical examination revealed a comatose child with facial twitching, hyperactive reflexes and a bilateral positive Babinski test.

A spinal tap showed a trace of globulin (Pandy test), 15 mgm.% protein, and 18 mgm.% sugar. The urine contained no acetone and gave a normal Sulkowitch reaction.

He responded spontaneously several hours after admission. On the third hospital day a fasting blood sugar was 57 mgm.% (capillary method). 17.5 grams of glucose were then given orally and the following glucose tolerance curve was obtained: ½ hour, 115 mgm.%; 1 hour, 95 mgm.%; 2 hours, 100 mgm.%; 3 hours, 112 mgm.%; 4 hours, 54 mgm.%. A cephalin flocculation test was normal. He was discharged eight days later on a regular diet.

Third hospital admission: He seemed well for six months until April 1948 when he had a mild upper respiratory infection followed by another convulsion (again just before breakfast). His temperature was 97.4° F., and he was semicomatose on examination. He was completely flaccid, with large, light-reacting pupils, and a questionable Babinski test. The blood sugar (venous) was 11 mgm.%, and response was rapid to intravenous glucose.

Several diagnostic tests were performed on this admission. The routine urines were normal, as was the blood count, Mantoux 1:10,000 and Kline test. The blood cholesterol was 300 mgm.%, blood chlorides were 470 mgm.%, and an electroencephalogram was normal. A glucose tolerance test was again done. The fasting sugar was 81 mgm.% (capillary blood). 18.2 grams of glucose were given orally, with the following results: ½ hour, 83 mgm.%; 1 hour, 121 mgm.%; 2 hours, 106 mgm.%; 3 hours, 81 mgm.%; 4 hours, 73 mgm.%; 5 hours, 65 mgm.%. At the fifth hour specimen 5 minums of adrenalin were given. Fifteen minutes later the blood sugar was only 55 mgm.%. The child appeared alert, however.

Several days later the fasting blood sugar was 77 mgm.% (capillary blood). Three units of regular insulin were then given intravenously. Ten minutes later the blood sugar was 65 mgm.% and he became comatose. Thereafter at ten minute intervals blood sugars were drawn and were 35 and 23 mgm.%, respectively. He remained comatose for 1½ hours and then slowly began to respond. The blood sugar at this time was 41 mgm.%. Between the second and third hour he became a little restless but refused oral feedings. Five minums of adrenalin were given but no response was noted. The sugar fifteen minutes later was only 44 mgm.%. Dramatic termination of the stupor was obtained with intravenous glucose.

Roentgenograms of the skull were normal, as was an abdominal flat plate. The bone age of the wrists, according to Todd, was normal. He was discharged on a high protein diet, but it was not rigidly followed.

Fourth hospital admission: He was seen again one month later. He had been abnormally sleepy on the morning of admission, and had "slept" through breakfast. He was unresponsive on examination and had a convulsion shortly thereafter. Once more, response was prompt to intravenous glucose.

Fifth hospital admission: One month following this he was readmitted for follow-up study. He had been well, and required only dietary adjustment before discharge.

Sixth hospital admission: He was seen again in July 1948, when, after having not eaten well for several days, he became comatose just before breakfast. On examination, he was flaccid and had some twitching of his eyes. His reflexes were hyperactive, but the remainder of the examination was normal. His temperature was 98.4° F., and he readily responded to parenteral glucose. A neurology consultant was unable to find any disorder, but the ophthalmologist described bilateral congenital cataracts with apparently normal fundi. Twelve hour fasting sugars (capillary blood) were taken on four consecutive mornings with the following results: 100 mgm.%, 87 mgm.%, 80 mgm.% and 76 mgm.%. Once again he was sent home on a high protein diet.

Seventh hospital admission: Several months passed to be followed by the seventh hospital admission. The shock was again pre-breakfast, and the venous blood sugar was 26 mgm.%. No further studies were done and he was discharged on dietary management.

Eighth hospital admission: His last admission was in November 1948 when he entered with symptoms of early shock. He had had a regular supper the night before, and the symptoms had occurred about 6 A. M., as previously.

He responded promptly to intravenous glucose. Again the examination was normal. The urine was positive for acetone, but contained no sugar. The blood sugar on admission was 21 mgm.%. An oral glucose tolerance test was performed after three days on a diet consisting of 140 grams of carbohydrate, 50 grams of protein and 70 grams of fat. The fasting sugar was 104 mgm.% (capillary). 19.4 grams of glucose were given and the following curve obtained: ½ hour, 112 mgm.%; 1 hour, 155 mgm.%; 2 hours, 89 mgm.%; 3 hours, 87 mgm.%; 4 hours, 102 mgm.%. An oral glucose tolerance test after three days on a low carbohydrate diet (80 grams of carbohydrate, 60 grams of protein, and 110 grams of fat) was then performed. The same amount of glucose was given orally and the blood sugars were as follows: fasting, 70 mgm.%; ½ hour, 155 mgm.%; 1 hour, 193 mgm.%; 2 hours, 125 mgm.%; 3 hours, 73 mgm.%.

No untoward symptoms were noted on either of these diets or tests, and he was dicharged on a diet consisting of 70 grams of protein, 80 grams of fat and 75 grams of carbohydrate. At present there have been no further hypoglycemic attacks, this being the longest period of time he has ever been free of seizures.

DISCUSSION

Etiology. Several etiological classifications of hypoglycemia are proposed and used by various authors[3-7]. Modifying Hartmann's[7] classification slightly, true hyperinsulinism may be compared to relative hyperinsulinism, true hyperinsulinism being noted in organic disease of the pancreas, in physiological islet cell hyperactivity and in hypertrophy of the islets of Langerhans. Among the causes of relative hyperinsulinism or functional hypoglycemia are the lack of storage of liver glycogen and the lack of development or breakdown of the carbohydrate regulatory mechanism, nervous and/or endocrine, without any demonstrable changes in the pancreas.[7, 8]

Any of these factors are capable of causing hypoglycemic episodes, but it is possible to exclude most of them with a fair degree of accuracy by the history, physical findings and laboratory

workup. Moreover, 70 per cent of all cases of spontaneous hypoglycemia in children are due to functional hyperinsulinism.[4]

The usual immediate exciting cause is a combination of decreased food intake, food loss and unusual energy expenditure, all of which strongly suggests that a lack of glycogen reserve, or poor glycogenesis may be the chief etiological factors. The frequent occurrence of ketosis and acidosis is in keeping with this.[5]

In our collected series fever associated with infection, fasting, overactivity and vomiting were commonly found as initiating an attack, and less than half of the cases seemed truly spontaneous.

Clinical Diagnosis. The diagnosis of functional hypoglycemia or relative hyperinsulinism is suspected in a child with repeated, non-progressive, hypoglycemic episodes interspersed with periods of complete remission.[2, 9] Those cases reported in the literature with a single isolated attack were not included in this collected series.

Most of the cases presented were males between one month and eight years of age. Between attacks the children were mentally and physically normal, and their fasting blood sugars were usually normal.

The hypoglycemic symptom-complex may show a few or many of such symptoms as flushing, sweating, drowsiness or restlessness and confusion, trembling, convulsions, dizziness or headaches, hunger, nausea, epigastric pain, cardiac palpitation and visual disturbances.[8, 10, 11]

On the neurological examination there may be nystagmus, variations in pupillary sizes and reactions, fixed stare, alteration in reflexes, muscular incoordination, muscle spasm, stiff neck, a positive Babinski or Kernig test, and, at times, aphasia, behavior changes, and even mania.[10]

According to Rector and Jennings[3] and Bennett[6] convulsions in a child occurring late at night, early in the morning before breakfast, several hours post-prandially, or after exercise should make one suspicious of hypoglycemia. Conn,[12] and Schneider and Ancona,[13] however, state that attacks almost never occur after midnight, do not occur pre-breakfast (2-8 A. M.), and are commonest 2-4 hours post-prandially. Conn[12] believes a skipped meal has no effect on causing a reaction and convulsions, when they occur, are of short duration, and always disappear spontaneously even though no food is taken.

In some respects the findings in our cases and the composite series differ from those of Conn and agree with Rector and Jennings.[3] Out of the collected series of 28 cases, 16 had attacks occurring in the early morning or before breakfast, and only 12 cases had symptoms occurring irregularly or post-prandially.

These episodes of functional hyperinsulinism differ from organic hyperinsulinism and hepatogenic hypoglycemia in that the latter two are progressive in frequency (unlike the series reported) and according to Conn are usual between 2 and 8 A. M.[4, 12] The organic type is usually precipitated by a skipped meal, or vigorous muscular exercise, and is not relieved by dietary manipulation.

Laboratory Diagnosis. In the functional type of childhood hyperinsulinism the fasting blood sugar between attacks is normal (70 mgm.% or above).[3, 12, 14] It remains normal even after a three-day carbohydrate restricted diet (normality here being considered 46-60 mgm.% glucose). Our two cases, after a three-day low carbohydrate diet of 50 grams of carbohydrate, 60 grams of protein and 110 grams of fat, revealed normal fasting blood sugars of 100 and 104 mgm.%, respectively. These figures help in distinguishing the functional type from organic and hepatogenic hypoglycemia, for in these cases fasting sugars are usually less than 50 mgm.%, and after three days of carbohydrate restriction usually range from 40 mgm.% or below.[4, 15]

The glucose tolerance test has also been found to be of some value in diagnosis by Conn[12], since it usually starts with a normal fasting level, but falls sharply to hypoglycemic levels in 2 to 4 hours in those cases with functional hyperinsulinism. However, in order to obtain more standardized and comparable glucose tolerance curves, he insists on a standard preparatory diet for at least three days before the test. This is done because a period of carbohydrate restriction, even in a normal person, causes marked delay in carbohydrate utilization in the glucose tolerance test. His diet consists of 300 grams of carbohydrate, 80 grams of protein and maintenance calories. Such preparation, he believes, will eliminate one cause for the different curves obtained in various patients and in the same patient.[4]

Rector and Jennings,[3] and Wilder,[17] however, feel that the glucose tolerance curves contribute little to the diagnosis of functional hypoglycemia, and Keating and Wilder[18] found that the

glucose tolerance tests were not helpful in four cases of adenomas of the islands of Langerhans, as marked variations occurred in the form and magnitude of the curves. In our patients the glucose tolerance tests were not characteristic of the extreme curves found in hepatogenic or organic hyperinsulinism, although there was a tendency for the curves of B.P. to be high, and those of H.S. to be about normal (Figs. 1 and 2). Analysis of the glucose tolerance curves in the composite series did not show any uniformity, except that none were extremely high or low, and all tended to fall in the middle range.

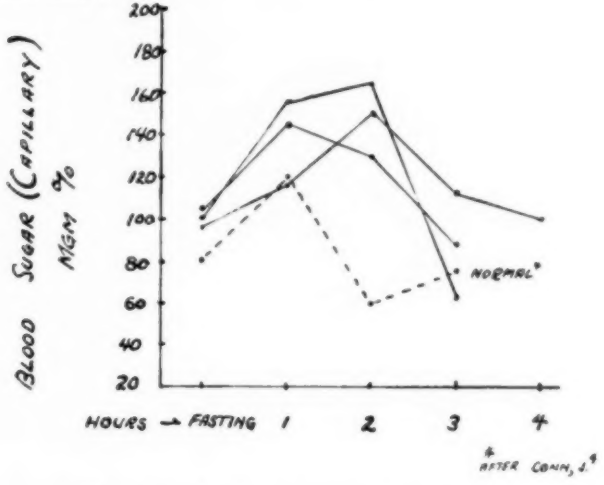

Fig. 1. Glucose tolerance curves of Case 1 (B.P.).

The practical importance of the dextrose tolerance curve, when used as a differential diagnostic point, lies in the fact that an extremely low fasting blood sugar followed by a high plateau curve with glycosuria and a gradual fall in 4 to 7 hours to hypoglycemic levels is the response usually found in hepatogenic hypoglycemia, while an extremely low fasting level with a low rise and a sharp fall to severely low levels in 2 to 5 hours is characteristic of organic hyperinsulinism.[4] Curves in the middle ranges, approximating the normal curve, are found in functional hypoglycemia.

The insulin tolerance test is also of value in diagnosing func-

tional hypoglycemia. This test (¼ unit of insulin per Kg. body weight, intravenously, after a twelve hour fast) according to Wier in an article by Rosenblatt,[19] does not affect the metabolically sound individual, but produces marked symptoms of hypoglycemia in those who "have subjective manifestations". Hartmann and Jaudon agree.[5, 20] Differentially, Womack[15] states that the insulin tolerance test generally has been normal in those patients with tumors.

Besides being of value in helping to distinguish functional hypoglycemia from organic hyperinsulinism, it is of some value in indicating either the pituitary, adrenal or pancreas as the organ

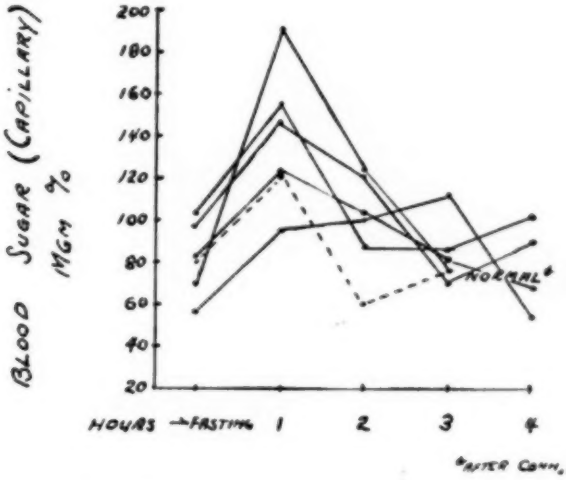

Fig. 2. Glucose tolerance curves of Case 2 (H.S.).

possibly responsible for the metabolic disturbance. Hyperfunction of the carbohydrate controlling factor of the anterior pituitary and certain components of the adrenal cortex is expressed by evidence of insulin resistance.[21, 22] Reduced function or absence of adrenal or pituitary secretions, or hyperinsulinism, is expressed by marked insulin responsiveness associated with an absent or delayed rise in blood sugar after the initial fall (hypoglycemia unresponsiveness).[21, 22] However, in "hypoadrenocorticism" (Addison's disease) there is, in addition, a slow initial fall of the blood sugar and

in "pan-hypopituitarism" the glucose tolerance test shows hyperglycemic resistance.[22] These latter additional points may help in distinguishing relative hyperinsulinism from the hypoglycemias of Addison's disease and hypopituitarism.

Theoretically, then, insulin hypersensitivity as seen in this test could be the result of a lack of storage of liver glycogen, or a lack of proper opposition to insulin activity by epinephrine or anterior pituitary hormone. Probably both explanations are correct.[5] In five cases of this collected series, which were given the insulin tolerance test, all showed marked insulin hypersensitivity, and all had a severe hypoglycemic reaction.

When epinephrine (3-5 minums) was given to relieve such symptoms, the rise in blood sugar was usually small in contrast to the elevation which follows the injection of epinephrine when unopposed by the previous injection of insulin.[5, 21] This also suggests poor mobilization of liver glycogen.[5] In this series the average rise in blood sugar after adrenalin injection was 13 mgm.%, which was much less than after giving the adrenalin following fasting or a glucose tolerance test. In the latter instances the average blood sugar rise was 44 mgm.% and 35 mgm.%, respectively.

Treatment. The immediate relief of the spontaneous hypoglycemic attack is obtained by glucose, either oral or parenteral. Adrenalin may be of value.

Prophylactically, treatment is dietary. Rector and Jennings[3] advise a moderately high carbohydrate diet augmented by midmeal snacks, or a mild ketogenic diet. Most of the cases reported with isolated hypoglycemic episodes were not treated by any special means after control of the initial attack. Hartmann,[5] Jaudon,[23] Bennett,[6] and Griffith,[24] however, treated those patients with repeated attacks by means of frequent feedings of a high carbohydrate diet. In many cases, however, results did not seem spectacular, for a number of the children continued to have attacks of hypoglycemia over a period of years.

Donnelly and Palmer,[8] Liebermann,[25] and Conn[4, 9] believe that diets high in carbohydrates are likely to intensify the syndrome, and therefore recommend a high protein diet. Neale,[26] for example, reported hypoglycemic attacks in three children. Two of the patients were not doing well on a high carbohydrate diet at the

time of writing, but one was benefited by a high fat, high protein, low carbohydrate diet.

According to Conn,[4] the therapeutic effectiveness of the high protein diet is due to the slow even rate of glyconeogenesis from protein, and the long period required for protein absorption. Protein, during metabolism, yields approximately 50 per cent of its weight as glucose, yet in normal persons and in cases with functional hyperinsulinism no significant rise in the blood sugar is demonstrable after a high protein meal.[12] Such a diet, therefore, satisfies the therapeutic objective of preventing high post-absorptive elevations of the blood sugar level which would stimulate the excessively responsive pancreatic islets to increased insulin production with the resultant secondary hypoglycemic dip.[4, 12] A high protein diet of 120-140 grams of protein, 50-75 grams of carbohydrate and maintenance calories has been suggested by Conn.[9]

Our two cases were unsuccessfully controlled on frequent feedings of a high carbohydrate diet, and had repeated hypoglycemic attacks. After the initiation of a high protein diet consisting of 70 grams of protein, 75 grams of carbohydrate and 80 grams of fat, no further attacks have been noted to date.

The use of pituitary, thyroid and adrenal extracts does not seem indicated in children.[3, 11] Epinephrine does not seem very effectual in those children with hypoglycemic attacks, as the blood sugar rise is only slight and transient.[3, 19, 20] The avoidance of infection and periods of fasting seems important.[27] The use of alloxan has recently been suggested by Talbot, Crawford and Bailey.[28] They reported on an eight-month-old infant with hypoglycemic convulsions of three months' duration. Extensive studies, including laparotomy, revealed no cause for these convulsions. She was treated with two courses of alloxan, and, after the second course, the hypoglycemic attacks ceased.

Some cases of spontaneous hypoglycemia have been operated in the search for pancreatic tumors. Very often there are no gross pancreatic changes of note. This has led to the formulation of certain criteria which, only when met, justify exploratory surgery. They are intolerance to fasting and over-fatigue, more or less progressive, persistent hypoglycemia of less than 50 mgm.%, and symptoms which are not relieved by dietary regulation, since it is well-known that medical management of organic hyperinsulinism is notoriously unsuccessful.[4, 5, 25, 29, 30]

SUMMARY AND CONCLUSIONS

Two children with spontaneous hypoglycemia have been presented and compared to a series of previously reported cases by various authors. All of these cases had repeated non-progressive hypoglycemic episodes interspersed with periods of complete remission. These attacks continued over a period of years or until the correct diagnosis was made, and dietary treatment initiated.

All of the cases seemed to indicate a lack of storage of liver glycogen and/or a lack of development or breakdown of the nervous or endocrine carbohydrate regulatory mechanism. Most of them revealed an immediate exciting cause of decreased food intake, or unusual energy expenditure, with the occurrence of a hypoglycemic attack in the pre-breakfast period, or occasionally, post-prandially.

Diagnosis depends on a suggestive history, especially in a male child, with normal physical findings between attacks, as well as normal fasting blood sugars on a standard diet, and a low carbohydrate diet. Laboratory studies for obvious pituitary, thyroid, adrenal and liver malfunction are normal. Urinalysis during the attack commonly reveals acetone or diacetic acid.

The glucose tolerance test, after dietary preparation, falls in the middle range, not showing the extreme height and rapid fall of hepatogenic hypoglycemia or the extremely low levels as found in organic hyperinsulinism. The curves, however, do not appear to be diagnostic. The insulin tolerance test reveals a marked hypersensitivity, with the rapid onset of a hypoglycemic reaction in all tested cases in this series, and an absent or delayed rise in the blood sugar after the initial fall. The adrenalin test, when given following the insulin tolerance test, shows only about one-half the rise in blood sugar, as compared to the blood sugar rise when the test is given after a twelve-hour fast or after a glucose tolerance test.

Immediate relief is obtained from glucose, while satisfactory prophylactic treatment seems to consist of a high protein, low carbohydrate diet, and the avoidance of fasting and unusual energy expenditure.

It appears, therefore, that there is no single diagnostic point, and that the diagnosis of functional hypoglycemia must rest on the combination of history, physical, laboratory tests and the response to dietary management.

The authors wish to thank Dr. J. Conn of the University of Michigan, and Dr. E. Gordon of the University of Wisconsin for their personal correspondence and suggestions regarding these cases.

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CONGENITAL MALFORMATIONS AFTER EXPOSURE TO MEASLES IN EARLY PREGNANCY. (Acta Paediatrica, Stockholm, 35:242, 1948). Hagströmer presents the histories of 2 infants with congenital malformation. One had a hare lip and partial cleft palate and the other had cleavage of the back palate, a rudimentary right ear placed a good distance forward on the cheek and a notably small chin. Both families had been free from such defects, but a brother of the first infant had had measles during the second month of the mother's pregnancy that resulted in the birth of the defective child. In the case of the second infant, 2 cases of measles had occurred in the family while the mother was in the second month of pregnancy. In both cases the pregnant women had remained free from measles, having had attacks during their childhood. Whether or not a causal relationship existed between the siblings' measles and the malformations described cannot be definitely decided.—*Journal A.M.A.*

CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York; Doctor Philip Moen Stimson, Cornell Medical School, New York, and Doctor John A. Toomey, Western Reserve University Medical School, Cleveland. Other interested medical schools are cordially invited to submit student papers for consideration.*

CONGENITAL ANOMALIES OF THE RECTUM AND ANUS*

A STUDY OF SEVENTEEN CASES AND COMPARATIVE REVIEW OF THE LITERATURE

ANTHONY VASILAS
New York.

In a study of approximately thirty thousand births, seventeen congenital anomalies of the rectum and anus have been found, two of which will not be referred to as complete data could not be obtained for these two cases. According to the studies of Ladd and Gross, one out of every five thousand births showed this phenomenon. Other studies show the ratio of one to ten thousand. According to this study, the proportion has been one out of two thousand. Even though this is an uncommon occurrence, it merits our attention.

The classification used to describe these anomalies was formulated by Ladd and Gross:

Type I. Incomplete rupture of the anal membrane or stenosis at a point 1 to 4 cm. above the anus.

Type II. Imperforate anus with obstruction due only to a persistent membrane.

Type III. Imperforate anus with the rectal pouch separated from the proctoderm. The rectal pouch may end blindly either in or above the pelvis.

Type IV. Normal anus and anal pouch with the rectal pouch ending blindly. There may be either a membranous obstruction between, or a separation of the anal and rectal pouches. When

* Submitted as partial fulfillment of the requirements of the course in Senior Pediatrics at the New York Medical College, Flower and Fifth Avenue Hospitals. Compiled from the files of Flower Hospital, Metropolitan Hospital and Queens General Hospital of the City of New York.

the pouches are separated, a cord of tissue without a lumen occasionally may connect them.

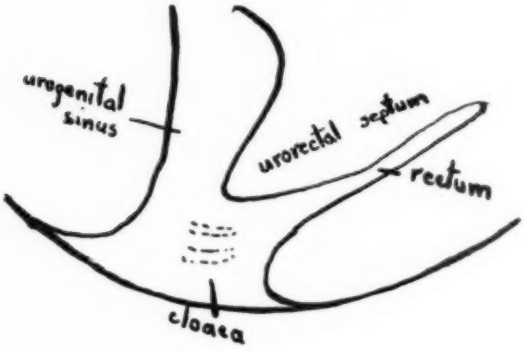
Embryology. The embryology has been formulated by Arey, and Ladd and Gross, which gives us a working knowledge.

The central portion of the alimentary canal, known as the mesenteron, is formed from the entoderm and consists at first of a simple tube which ends blindly anteriorly and posteriorly. The tube represents only the mucous membrane. Later it becomes enveloped in a layer of mesoderm which differentiates into two portions, the outer forming the peritoneal covering, while the inner forms the muscle and connective tissue elements. An invagination of ectoderm takes place later at the two ends—anteriorly at the mouth called the stomodeum and posteriorly at the proctoderm, which constitutes the anal orifice. At five weeks in the embryo the intestine and urogenital sinus empty into a common opening which is known as the cloaca.

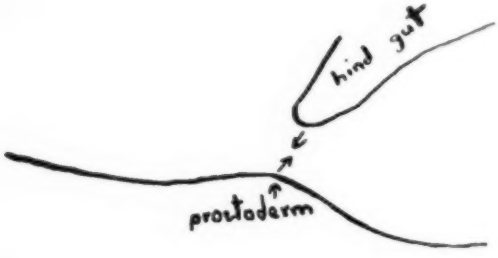
At six weeks the urorectal septum grows caudally dividing the cloaca. This is completed at nine weeks. The ventral division gives use to the bladder and a greater portion of the urethra. In the female, you get the Muellarian duct system.

The posterior division forms the anal canal. A small pit forms in the perineum called the proctoderm which folds inward until it joins the hind gut. This infolding occurs when the membrane separating them and known as the anal membrane ruptures.

The sphincters develop from the mesenchyme and are independent of this above growth. It is obvious that any arrest or perversion in the downward growth of the urorectal septum, which should separate the urogenital tract from the gastro-intestinal tract, will result in fistulas.



Fistulas. Out of the fifteen cases reported, seven had associated fistulas. The fistulas found in the male are rectovesical, rectourethral and rectoperineal, the commonest being the rectourethral.



The following tables illustrate the distribution found in this study:

	Rectourethral Rectovesical	Rectoperineal	Total
Males.....	3	1	4

The fistulas found in the female are rectovaginal, rectovesical, rectofossa navicularis and rectoperineal, the commonest being the rectovaginal.

	Rectovesical	Rectovaginal	Rectofossa Navicularis	Rectoperineal	Total
Females.....	0	3	0	0	3

Associated Anomalies (not including fistulas). In this series of fifteen cases, nine had associated anomalies, or sixty per cent.

In the series reported by Ladd and Gross, twenty-six per cent were found to have anomalies, and in the series by Berman, fifty-six per cent were found to have anomalies. All of our cases were found to have more than two associated anomalies.

A comparative study is illustrated below:

ASSOCIATED ANOMALIES

Type	Berman 23 cases		Ladd & Gross 162 cases		Present Study 15 cases	
Congenital heart	4	17%	8	4%	1	6%
Hare lip or cleft palate	0		3	2%	0	20%
Atresia of the small intestine	0		4	2%	3	6%
Double vagina & bifid uterus	2	8%	3	2%	2	13%
Spina bifida	1	4%	2	1%	1	6%
Absence of kidney	1	4%	2	1%	0	
Anomaly of bladder & ureter	2	8%	2	1%	4	26%
Horseshoe kidney	0		1	.06%	2	13%
Polycystic kidney	0		2	1%	0	
Mesenteric anomaly	0		2	1%	1	6%
Meckel's diverticulum	1	4%	1	.06%	2	13%
Malrotation of the gut	0		0		1	6%
Microcephaly	0		0		1	6%
Supernumerary digits	0		0		2	13%
Atelectasis of lungs	1	4%	0		1	6%

Distribution of the Anomalies as Shown by Present Study and Past Studies. The following table compares the distribution of the four types of rectal anomalies of past studies with that of the present study.

Name of Study	Type I		Type II*		Type III		Type IV		Total No. of Cases
Ladd & Gross	21	13%	6	3%	117	71%	18	11%	162
Dymytryk	5	33%	0	0%	10	66%	0	0%	15
Halsted	0	0%	2	8%	17	68%	6	24%	25
Lee	4	25%	0	0%	11	68%	1	67%	16
Crowell & Dulin	3	11%	6	23%	16	61%	1	37%	26
Present Study	4	26%	3		8	53%	0	0%	15

* Type II cases are easily treated. They may not be severe enough to warrant hospitalization. As a result the number of such cases in hospital files may be much smaller than the number of cases in existence.

Symptoms and Signs. The symptoms and signs vary according to the degree of intestinal obstruction and to the following factors:

1. The type of anomoly.
2. Whether or not there are any fistulas present.
3. The type of fistula and size of fistula.
4. The associated anomalies.

Frequently it is the nurse who discovers the difficulty when she first attempts to take the temperature of the child. It is also noted that no meconium has been passed and the diaper is not soiled. Meconium may be noted discharging from the urethra, vagina or a perineal fistula. After 24 to 48 hours you get the signs and symptoms of intestinal obstruction, such as distention, vomiting, borborygmus, irritability and dehydration.

Type I. These patients come to the clinic later than those with complete obstruction. It varies from days to months to years. The stools are usually ribbon-like. Distention is often seen in this type. Sometimes these patients never come because they have no symptoms.

Type II. These patients are seen within the first few days. No meconium usually noted. A small bulging may be noted at the site where the anus should be.

Type III. Symptoms in this group depend upon whether or not the fistula is present.

(a). If there is no associated fistula, you will get symptoms of intestinal obstruction.

(b). If there are associated fistulas, the signs and symptoms depend upon the size of the fistula. If small, you will get signs of obstruction. However, if it is large, you will get no symptoms and, therefore, surgery may be delayed.

Type IV. This is often difficult to detect because a normal opening is present. Thus patients are diagnosed much later than those of Types II and III. Type IV cases are recognized about the fourth or fifth day. By that time progressive signs of intestinal obstruction are noted. This delay of recognition makes risk of operation greater in this type than for other types.

X-ray Findings. Wangensteen and Rice, in 1930, described a method of determining the position of the blind rectal pouch in patients with imperforate anus.

The infant is turned upside down and a flat plate of the abdomen and pelvis is taken, with an opaque marker, usually a thermometer, at the usual site of the anal site. Gas in the intestine rises and outlines the rectal pouch giving the location in the pelvis. This technique is good only after twenty-four hours when the gastrointestinal tract has acquired some air.

Berman, on the other hand, has described a good method for

the first twenty-four hours, i.e., fluoroscopy. By moving the infant into various positions and gentle massage of the abdomen, gas may be forced into the blind pouch.

Treatment. Treatment of these congenital anomalies is obviously surgical and varies with the type of malformation present. For greater surgical detail the articles of Berman, Harken Crowell and Dulin are recommended.

Rules to be followed in treatment:

1. Make an accurate diagnosis.
2. Avoid colostomy whenever possible. Mortality in this group is high, especially in the newborn.
3. Dissection should be made from below, if possible.

Type I. Repeated dilatations are made, gradually increasing the size of the dilators. This must be kept up from weeks to months. When the opening in the anal membrane is small, obstruction may be relieved by a cruciate incision followed by dilatation.

Type II. Simple cruciate may suffice. If this is not entirely satisfactory, then anal dilatations are instituted. Crowell and Dulin have reported that after an unsuccessful incision and dilatation, a colostomy followed, as a result of which the patient improved.

Type III. The form of treatment to be instituted in this type depends upon the rectal pouch and also the presence of fistulas and their size.

(a) If there are no associated fistulas, the type of operation depends upon the position of the rectal pouch in the pelvis. If the blind pouch is less than 2.5 cm. from the proctoderm, then the perineal approach is preferable. This (proctoplasty) is ideal because it immediately creates an anal opening in the normal position.

If the blind pouch is over 2.5 cm. from the proctodermal plate, then a colostomy is indicated. Colostomy is also the treatment of choice when the patient is severely dehydrated, distended and tympanitic. Mersheimer prefers to do the colostomy in the transverse colon, because when the perineal procedure is used at a later date to form the anus, then surgery becomes a much smaller problem than if the colostomy were done below the umbilicus. In the cases with a colostomy, the question arises as to what would be the most propitious time to perform the perineal operation. According to some, it should be done early because failure

to do so will result in disuse atrophy of the sphincter. The second school of thought is to perform the operation later when the structures are better formed and more amenable to surgery.

(b) If you have fistulas present, and they are large enough, surgery may be delayed. However, when the fistula is small, there will be signs of obstruction. If the child is unable to stand surgery, then simple dilatation of the fistula may be used temporarily. Otherwise, the procedure of choice is to do a colostomy. In my opinion, a proctoplasty in such a case, and repair of the fistula will increase the operative mortality.

Type IV. The treatment of this type of anomaly is usually colostomy. However, if the obstruction is membranous, incision and dilatation from below may suffice.

Comparison of Mortality Rates. It must be noted that these mortality rates are not surgical mortality rates.

	Ladd & Gross		Crowell & Dulin		Dymytryk		Berman		Present Study	
TYPES	No. of Patients	% of Mortality	No. of Patients	% of Mortality	No. of Patients	% of Mortality	No. of Patients	% of Mortality	No. of Patients	% of Mortality
I	21	9.5%	3	0%	5	0%	1	0%	4	50%
II	6	16.6%	6	4.3%	No cases		2	50%	3	33⅓%
III	117	24.8%	16	13%	10	70%	2	0%	8	62.5%
IV	18	61%	3	0%	No cases		11	90%	No cases	

Surgical Mortality on Present Series. The four deaths attributed to surgery were all of Type III. These patients lived for 2, 21, 12 and 40 days, respectively. The first two cases died of peritonitis, the third of postoperative sepsis and the fourth of intestinal obstruction and peritonitis, following a second colostomy, which was performed to relieve the intestinal obstruction which had formed since the first colostomy.

TYPE	Mortality Rate
I	0%
II	0%
III	57%

SUMMARY

A series of seventeen cases of congenital anomalies of the rectum and anus have been reviewed. Of the seventeen cases, two could not be included in the discussion because of insufficient data.

Three cases were prematures. Seven of the fifteen discussed cases had associated fistulas. Nine had associated anomalies other than fistulas. Nine died, raising the mortality rate to sixty per cent. Of the nine deaths, five were attributed to associated anomalies and four to surgery.

The literature has been thoroughly reviewed and compared with the present study.

I wish to extend many thanks to Dr. Mersheimer for his very helpful suggestions.

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Dymytryk: Congenital Malformations of the Anus and Rectum. Arch. Surg., 50: 253, 1945.

NEUROBARTONELLOSIS. (Revista Médica Peruana, Lima, 21:641, Oct. 1948). The subject of this report is a girl 15 years of age with the gravest type of neurobartonellosis. The disease began with fever and an eruption. Fever was followed by rapidly progressive anemia, fronto-occipital headache, general muscular pain, pain in the bones, unilateral disesthesia, tremor of lips, blurring of vision, dizziness, increased tendon reflexes, acute epigastric pain, nausea, vomiting and dyspnea. The blood contained 60 per cent of parasitic cells. Treatment consisted of intramuscular injections of penicillin in daily doses varying between 200,000 and 600,000 Oxford units, up to a total dose of 5,000,000 units in twenty-two days. Penicillin caused disappearance of Bartonella organisms from the blood, controlled anemia, favorably changed the course, duration and acuteness of the disease and controlled all of the clinical and nervous symptoms of the disease.—*Journal A.M.A.*

CLINICAL-PATHOLOGICAL CONFERENCE

WILLARD PARKER HOSPITAL, NEW YORK

Meeting held June 2, 1949

DR. PHILIP MOEN STIMSON, presiding.

TUBERCULOUS MENINGITIS

Dr. Tucker presented Case No. 1800, a 9½-year-old Negro boy, who was transferred to Willard Parker Hospital from another hospital on April 12, 1949.

In essentially good health until December 1947, he was admitted to a hospital for the first time because of pain and inability to move his neck. X-rays revealed no fracture or subluxation, but a destructive arthritis of C1 and C2 were noted. Mantoux 1/10,000 was positive. X-ray of chest and gastric washings were negative. A successful fusion of the first four cervical vertebrae was performed. He did well for 15 months until early in April 1949, when he was readmitted to the previous hospital because of cough and headache for 8 days. For a week before admission, he had a cough, running nose, headaches and intermittent fever. He was given sulfadiazine in the pediatric clinic without apparent effect. For that reason he was admitted here on April 4, 1949. Physical examination revealed a well-developed child in no distress with clear sensorium. The range of motion of the neck was limited due to the spinal fusion. The knee jerks were diminished. Kernig and Brudzinski signs were negative.

Pertinent laboratory findings included, hemoglobin 10.4 gm., R.B.C. 3.5 million, W.B.C. 12,300, with 67 per cent polys, 22 per cent lymphs, 10 per cent monocytes. Spinal fluid: 250 R.B.C., 17 W.B.C. with 13 lymphs, protein 496 mgm., sugar 63, chlorides 580. Therapy consisted of sulfadiazine and penicillin. The patient gradually became lethargic, vomited occasionally, and had a daily rise of temperature to 103° F. Five days after admission lumbar puncture revealed 1700 W.B.C., 95 per cent lymphocytes; 2 acid-fast bacilli were found on smear. He was then started on streptomycin, 400 mg. intramuscularly every 8 hours (for a total of 4 gms.) and 100 mg. daily intrathecally (for a total of 400 mg.).

The patient was then transferred to Willard Parker Hospital on April 12, 1949, with an admission temperature of 101.2° F.;

pulse 110, respirations 18. He appeared chronically ill, lethargic, but responded to stimuli. Pupils were dilated and reacted sluggishly to light. The fundi were normal. The neck was fixed by a spinal fusion, the lungs were clear. Liver and spleen were not palpable. Abdominal reflex was absent on the right. Cremasterics were absent bilaterally. Patellars were diminished bilaterally. Ankle jerks were active. No clonus was present. Extensor plantar response was present on the right. Kernig's was negative.

Laboratory Findings. Urine, negative. R.B.C. 3.5 million; hemoglobin 9 gm.; W.B.C. 13,500 with 66 per cent polys. Spinal fluid: cells 1875, protein 1145 mgm. Sugar, 54. Mantoux, positive 1/10,000.

The patient was given streptomycin. In addition, he received promizole 0.5 gm. every 6 hours by mouth and was maintained on gavage feedings and parenteral fluids.

Four days after admission, the patient became jaundiced; urine contained 4 plus urobilin and no bile. R.B.C. dropped to 1.8 million. Cell volume 19. Platelets remained within normal limits. W.B.C. rose to 30,000. Icteric index—96. Positive indirect van den Bergh. Negative Coombs test. The promizole was discontinued and the icterus slowly cleared. The spinal fluid sugar remained normal for 5 days, then suddenly fell to 11 mg. The protein reached a maximum of 3,000.

The patient graduallly became comatose although afebrile; superficial reflexes were lost, deep reflexes diminished, and Kernig became positive. On the sixteenth day after admission, the temperature suddenly rose from 97° to 103° F. when the patient expired.

Autopsy Findings. The body was that of a well-developed, fairly well-nourished boy, 9-year-old.

A surgical scar about 10 cm. long extended from the base of the skull to the region of the fifth cervical vertebrae. Another scar, 7 cm. long, was present posteriorly along the left iliac crest. The brain and spinal cord were removed. The brain weighed 1230 gms. The surface of the hemispheres was rather edematous with flat pale convolutions. The meningeal veins were engorged, but there was no meningeal edema over the hemispheres and no tubercles could be seen with the naked eye. At the base of the brain, however, there was a thick fibrinous, mucoid exudate which cov-

ered the entire brain stem on the lower surface and extended forward around the chiasm. There was a partial block around the foramen magnum. The floor of the third ventricle in the area of the infundibulum bulged slightly. A few small tubercles could be seen on the basal aspect of the hemisphere. On section, there was no significant distention of the lateral ventricles. The third ventricles of the aqueduct were only slightly distended. The fourth ventricle was only moderately widened but was filled with a complete cast consisting of thick creamy white exudate which also surrounded the choroid plexes. The roof of the fourth ventricle was adherent to the base of the cerebellum. No tuberculomata and no gross softening were found. The subarachnoid space around the spinal cord was distended by thick exudate which apparently contained much fibrin.

On opening the chest cavity a group of fairly large lymph nodes was found on the right side at the angle of the trachea and the right main bronchus. A small caseous lymph node was found in the right hilus. Numerous sections throughout both lungs failed to reveal any primary focus of tuberculosis, on gross or microscopic examination. However, the presence of caseous lymph nodes in the right tracheobronchial angle and in the hilus of the right lung and nowhere else indicated that the right lung probably was the site of a primary tuberculous infection. It is possible that the primary focus has healed without any trace. No evidence of tubercles was found in the abdominal organs or lymph nodes on gross or microscopic examination.

The lack of evidence of recent hematogenous spread suggests that the meninges have been infected by either direct extension or drainage from tuberculous foci in the vertebrae rather than by the hematogenous route.

We were asked to preserve the body in the best possible way for the burial and because of that we could not obtain the bodies of the cervical vertebrae for examination.

Microscopic slides of some of the lesions were projected. Sections from the convexity of the brain showed no true tubercles in the meninges. Occasional groups of lymphocytes and mononuclear phagocytes were seen in the sulci. A few tiny tubercles were found around the meningeal blood vessels of the convolutions at the base of the hemispheres. The tuberculous exudate around

the chiasm was shown. The walls of the fourth ventricle were found to be invaded by a few small tubercles. The choroid plexus of that ventricle was embedded in a tuberculous exudate and contained tubercles in its stroma.

In the spinal cord, the nerve roots were enveloped in a tuberculous exudate, and a few tiny tubercles were found within the white matter of the spinal cord.

The caseous lymph nodes showed extensive deposits of calcium and a great thickening of their capsules. However, a few tubercles were still identifiable.

Sections from the lungs showed a nontuberculous bronchitis. Minimal amounts of blood were present in the lumen of some alveoli, and an increased number of lymphocytes were within the alveolar walls, but no evidence of recent or old tubercles could be found.

NEUROBLASTOMAS. (Nordisk Medicin, Stockholm, 40: 2211, Nov. 26, 1948). In the 3 cases of neuroblastoma reported in children aged between 1 and 6 with typical localization in the adrenal medulla, the clinical picture was dominated by cranial metastases. Tumor cells demonstrated in the bone marrow and roentgenologically established metastases to the bone system facilitated the diagnosis. Death from cachexia occurred after two and a half to six months. Tho says that in differential diagnosis myeloblastic leukemia is first to be considered; the clinical picture together with the sternal puncture and roentgen picture as a rule clarifies the situation. In 2 of the cases signs of lively blood regeneration with high reticulocyte count were found; in leukemia there is most often little tendency to blood regeneration. Wilms' tumor seldom leads to bone metastases; urography, often positive in this tumor, is usually negative in neuroblastoma. Ewing's tumor is rare in patients aged under 4. Metastases generally give the first and characteristic symptoms in neuroblastomas. The tumors are radiosensitive. In Farber's series of 40 patients 10 are living after three to eight years, and Farber would revise the earlier hopeless view of the prognosis. Irradiation cannot hinder the development of metastases, which may be latent several years, but they also are radiosensitive. Irradiation of skeletal metastases has not prevented recurrence.—*Journal A.M.A.*

BOOK REVIEW

CHILD HEALTH SERVICES AND PEDIATRIC EDUCATION. Report of the Committee for the Study of Child Health Services of the American Academy of Pediatrics. Cloth. Illustrated. Pp. 270. Price $3.50. New York: The Commonwealth Fund, 1949.

This book is a statistical study of the medical services available to the infants and children of the United States and the type and amount of pediatric education that is found in the medical schools. In the final analysis the mass of charts and graphs illustrates vividly what most of us already know or suspect, viz., (1) that specialists tend to congregate in large urban centers, (2) the greater portion of infant and child care is in the hands of the general practitioners of the country who incidently have done a commendable job, and (3) the better the economic position of a particular state in question the better is the service both public and private available to the infant and child of the state. The facts and figures bring to the forefront the inequalities of medical service and the inadequacy of pediatric education in the medical schools. The next and greater effort will be how to correct these deficiencies. Statistics can at times be misleading but they can also place in the proper prospective some interesting facts, e.g., "accidents are now responsible for about 1 in every 4 deaths among children beyond the age of one year, outranking every other cause of death in this age group. Today rheumatic heart disease is at the top of the list of causes of death from disease. A rather surprising finding is the entrance of cancer, including leukemia, into the picture as one of the leading causes of death among children."

MICHAEL A. BRESCIA, M.D.

FOLIC ACID IN CELIAC DISEASE. (Archives of Disease in Childhood, London, 23: 220, Dec. 1948). Hay reports on 22 infants and children who had celiac disease and were treated for a period with a low fat and high protein diet, liver extract and vitamins. Folic acid was then added to the treatment for a comparable period. The clinical condition of the children during these periods was compared by observations on rate of gain in weight and on the character of the feces as seen with the naked eye. No conclusive evidence was obtained of any beneficial effect of the folic acid.—*Journal A.M.A.*

The year that got away—

Long ago, he'd planned the year, the day, the hour of his retirement.

But now, a year beyond that date, his desk is still open . . . the weekday trout still in the brook.

What happened? Unexpected expenses . . . Nickie starting college . . . the last of Mom's hospital bills. He never really figured it out. But the happy day he planned was no longer in sight.

A lot of years are getting away from a lot of people . . . because they don't have a plan which helps them save money *regularly*. But there *are* people who are making the most of the years, by investment in United States Savings Bonds.

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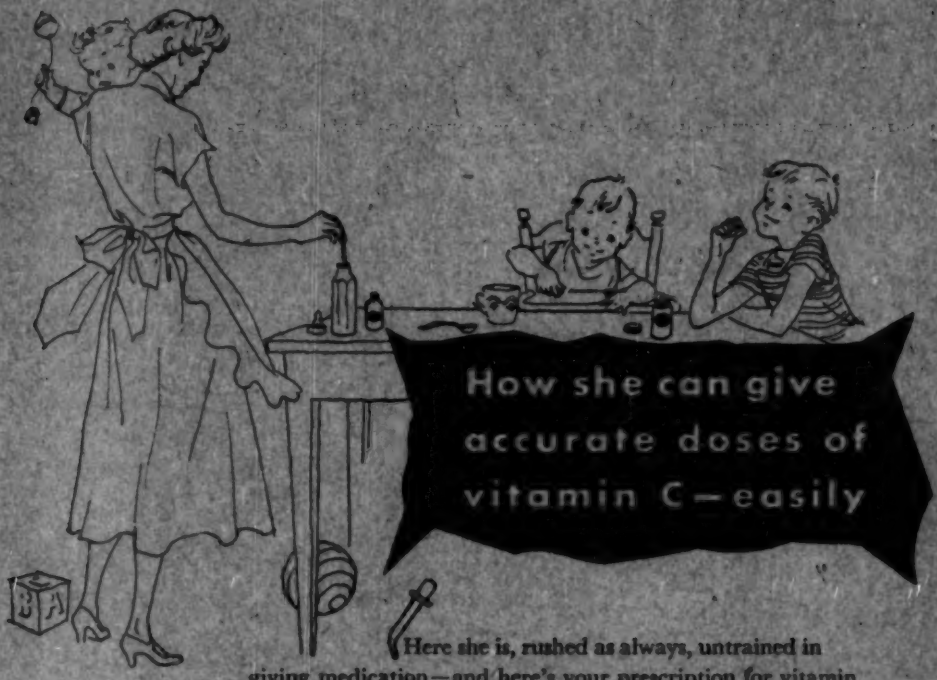

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With the dropper from the Cecon bottle, the mother measures out, let's say, four drops. This contains 10 mg. ascorbic acid (100 mg. per cc.), regardless of whether the bottle is freshly opened or has been on the pantry shelf for months. Mixed with formula or other food, it's tasteless, miscible. No tablet chips in nipple or cup. Supplied in dropper-top bottles of 10 cc. and 50 cc. Cecon *Dulcet* Tablets, newest Abbott candy-like specialty, contain 50 mg. ascorbic acid in each delicious, easily chewed tablet. Supplied in bottles of 100 tablets. Children accept them as readily as candy.

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